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THE PATHOLOGICAL YARDSTICK

ITS ACCURACY AS AN INSTRUMENT FOR MEASURING ERRORS IN CLINICAL, ROENTGENOLOGICAL, AND SURGICAL DIAGNOSIS OF GASTRIC LESIONS

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EIGHT microscopic sections of organic gastric lesions, chosen from surgical and autopsy specimens were presented to some or all of the following pathologists. (A most hearty co-operation of all the pathologists consulted has been one of the high lights in my professional experience. Therefore, above all things I am anxious that this contribution should be presented in such a way that it will offend none of them.)

Dr. James Ewing, Memorial Hospital, New York
Dr. Fred W. Stewart, Memorial Hospital, New York
Dr. I. Lacassagne, Curé Institute, Paris, France
Dr. Ivan Bertrand, Paris, France
Dr. Paul Klemperer, Mt. Sinai Hospital, New York
Dr. Paul W. Aschner, Mt. Sinai Hospital, New York
Dr. E. Thompson Bell, University of Minnesota, Minneapolis, Minnesota
Dr. A. C. Broders, formerly of the Mayo Clinic, University of Virginia
Dr. A. P. Stout, Columbia University Medical Center, New York
Dr. A. M. Pappenheimer, Columbia University Medical Center, New York
Dr. Nathan C. Foot, Cornell University Medical Center, New York
Dr. Louis H. Jorstad, Barnard Free Skin and Cancer Hosp., St. Louis, Missouri
Dr. Frank W. Konzelmann, Temple University, Philadelphia, Pennsylvania
Dr. Harrison S. Martland, Newark City Hospital, Newark, New Jersey
Dr. John W. Gray, Newark, New Jersey
Dr. J. W. McWhorter, French and Bellevue Hospitals, New York
Dr. Charles F. Geschickter, Baltimore, Maryland
Dr. P. Masson, Montreal, Canada
Dr. Louis C. Simard, Montreal, Canada
Dr. L. J. Rhea, Montreal General Hospital, Montreal, Canada
Dr. W. L. Robinson, Toronto General Hospital, Toronto, Canada
Dr. T. B. Mallory, Boston City Hospital, Boston, Massachusetts
Dr. Fred. Parker, Boston City Hospital, Boston, Massachusetts

Each pathologist was asked to examine the identical sections, to answer the three following questions, and to allow their answers to be published.

1. Is the lesion malignant? Yes or no.
2. What is the type of lesion—carcinoma, sarcoma, etc.?
3. On what criteria did you base your opinion?
   - A. Arrangement of cells.
   - B. Size and shape of cells.
   - C. Nuclear changes.
   - D. Changes in the chromosomes.
   - E. The manner in which the cells take the stain
   - F. Invasion of adjacent structure.
   - G, H, I. Any other criteria.

If a teacher, he was asked if he would pass a student who could not differentiate a carcinoma from a sarcoma.

A definite diagnosis by any method, even though it is occasionally wrong, is more to be desired than an equivocal one. There are four distinct methods of diagnosis, namely: clinical, roentgenological, surgical exploration, and pathological. The relative value of a diagnosis from the clinical, roentgenological, and surgical findings is a controversial subject. No method is infallible but a microscopic examination has settled the question of diagnosis in each case where it has been possible to obtain it. Thus pathology has become the yardstick used to measure all other diagnostic errors.

In the early days of gastro-intestinal roentgenology when there was great skepticism as to the accuracy of the method, any old yardstick would do to measure *its* failures. Of my first 5 consecutive cases of x-ray diagnosis of gastric cancer, 3 were shown to be wrong (see Fig. 1): 1 as measured by the clinical yardstick, and 2 by surgical exploration, namely, the surgical yardstick. This was most discouraging, but even then I retorted that none of these cases had been disproved by microscopic examination, namely the pathological yardstick *on which we all depend*. However, Father Time wielded his carcinomatous reaper on all 3 of these cases thus changing my percentage of something over 60 per cent error to 100 per cent accuracy on my first 5 cases.

Brewer's report of 27 cases, presented before the American Surgical Association (1) in which x-ray errors were measured by the surgical yardstick did more to establish gastro-intestinal roentgenology than any other work with which I have been associated. This series of cases of Brewer's and subsequent experience showed that the x-ray diagnosis of gastric ulcer is as easy and accurate as the diagnosis of fracture, and furthermore that gastric cancer can be differentiated from ulcer by x-ray as readily as the red cards can be separated from the black in a playing deck. Try this for yourself (see Fig. 2). In every playing deck there is a joker and advertising card. By this time you have probably found the x-ray joker in Figure 2.

In most cases of cancer the microscopic criteria is so characteristic that the diagnosis is readily made, but there are also pathological jokers (see Fig. 3).

The report of these early successes in the diagnosis of gastric cancer does not mean that I have not made mistakes both of omission and commission. The most common cause of the error of omission was the failure to include the fundus or fornix in the examination. Lack of the knowledge at the time the examination was made, that a simple ulcer never involves a greater curvature, caused me to misinterpret a case of ulcerating carcinoma as an indurating ulcer. The prevalent erroneus conception that rugæ radiating from a crater indicate a non-malignant lesion caused my downfall in another case which was reported in our book *Radiological Exploration of the Mucosa of the Gastro-Intestinal Tract* (4) and also in the *American Journal of Surgery* (3). Misinterpretation of lack of pliability of a localized area on the lesser curvature was perhaps the most justifiable mistake, if one can speak of a mistake as justifiable. I considered it due to a scar from an ulcer whereas it was really early carcinomatous infiltration (4).

In 1912 I made a diagnosis of ulcer on the lesser curvature and the patient subsequently died of carcinoma. Apparently the carcinoma developed at a different region, but this could not be definitely established.

The most serious mistake that I have made, at least in recent years, was in a patient who was not only a patient but a friend: Mr. D. B., 60 years plus, suffered from symptoms rather significant of gastric ulcer. When I first saw him professionally he was scheduled to have a gastro-enterostomy the next day for a gastric ulcer in the pyloric canal. I then considered that the ulcer was probably non-malignant and recommended at least further rest in bed to allow for subsequent series of films. This second series, and also others over a period of 3 years speak for themselves, especially with the legends (Fig. 4 A, B, C, D).

As I now review these series of films and especially as I compare them with a case to be reported hereafter (Case I) I marvel at the queer quirks of man's mentality and philosophize on why, on almost identical findings, one sometimes makes a definite diagnosis of carcinoma as I did in Case I whereas in this

[1] These cases were originally reported in the Journal of the American Medical Association.

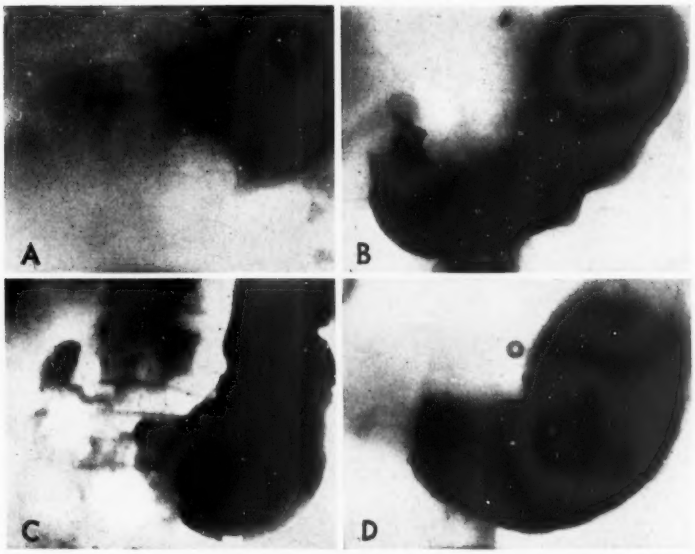

Fig. 1. A, B, C, and D illustrate 4 of the first 5 cases in which I made a positive diagnosis of gastric cancer. A, A positive roentgenological diagnosis of carcinoma was proved correct by the yardstick of surgical exploration. The patient died within a week. Considering that this patient was so free from symptoms that she was bored at having to have the examination, I have often wondered whether I did a good or bad job in diagnosing this first case of cancer. B, A positive roentgenological diagnosis of a pyloric cancer was shown to be wrong by the *clinical yardstick*. The patient improved and was practically free from symptoms 9 months after the examination. C, A positive roentgenological diagnosis of a large pyloric cancer was shown to be wrong by the yardstick of *surgical exploration* and a gastro-enterostomy. Mayo found two ulcers with glandular involvement and nodules in the liver but reported that "malignancy was not established" and therefore our roentgenological diagnosis was wrong. D, A positive roentgenological diagnosis of a small operable cancer. Surgical exploration proved that the clinical diagnosis of a small benign lesion was correct and the patient improved after a gastro-enterostomy. Therefore the roentgenological diagnosis of cancer was again wrong.

Thus, as measured by the clinical and surgical yardsticks something over 60 per cent of our first 5 cases were wrong, but they all died of carcinoma thereby making our first 5 cases 100 per cent correct instead of 60 per cent in error.

case I was either equivocal or in favor of non-malignancy. In this case the fact that the patient was a friend as well as a patient led to the wish being father to the thought. Another reason was that very shortly prior to this I saved a friend of mine who was a doctor from losing the pyloric end of his stomach because it was considered malignant. And the third reason, which I must perhaps shamefully confess, is that I had been recently irritated by the statement that all ulcerative lesions in this region should be considered malignant and therefore rather bent over backward in the opposite direction, in this case.

The points to be learned from this failure are either not to treat your friends or else to treat them as patients rather than friends, to stick more strictly to the rules that you have laid down concerning the diminution and disappearance of the crater in a certain period of time, namely a month, and the third and most important is that while the roentgenological examination may be used to determine whether a lesion is operable or inoperable, that factor should be entirely divorced from the diagnosis.

I believe that I should have made a positive diagnosis of carcinoma at least at the time of

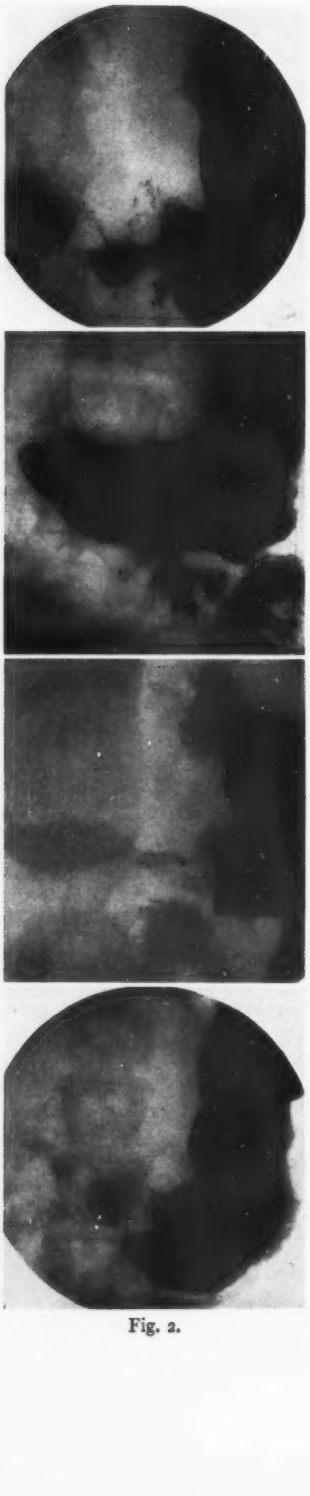

Fig. 2.

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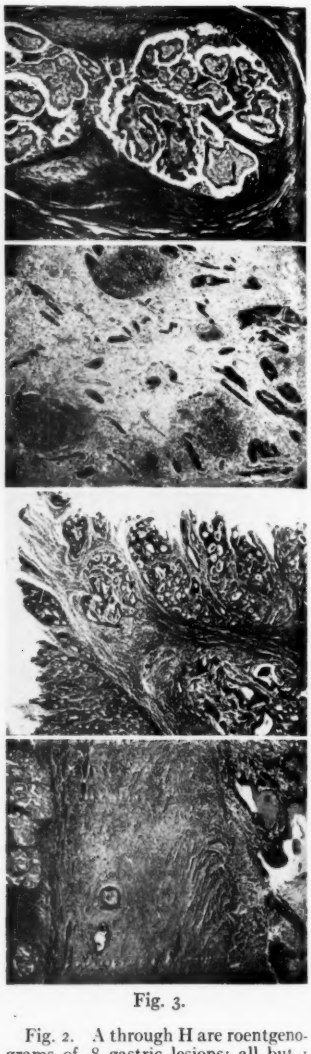


Fig. 3.

Fig. 2. A through H are roentgenograms of 8 gastric lesions; all but 1 of these were made on glass plates and single screen, most of them having been made before the battle of the Mississippi Medical Association in 1912 when I first advocated the direct detection of gastro-intestinal lesions in roentgenography and where it was stated by a representative of a clinical group of great authority that roentgenology was all right for bones, kidneys, and perhaps lungs but they had proved it to be no good for gastro-intestinal lesions. Look at the repro-

the second examination and that I should not have confused the issue of a definite diagnosis of cancer with the decision of whether to operate or not to operate because of an adverse constitutional condition of the patient. In this case the clinical condition of the patient seemed to contra-indicate so radical an operation as a gastric resection, but this was not the fact because Dr. Fred Rankin of Lexington, Kentucky, successfully performed a gastric resection which prevented the patient from succumbing to carcinoma before he died of a cerebral hemorrhage about a year and a half later. This error is bad enough but in part it is redeemed by the fact that of his 5 year span 3½ years of this extension of life was due to our error and 1½ years' extension of life due to Dr. Rankin's successful operation which carried the patient through to a period where he succumbed to a lesion which is considered one of the natural causes of death. aging arteries.

However, this article is an excellent opportunity of confessing one of my most serious errors and I now appreciate the relief afforded by a confession.

While attempting to correlate the roentgenological findings with gross pathology in order to establish the principles on which roentgenological diagnosis is based, gross surgical and anatomical specimens or microscopic sections or both were obtained in 87 consecutive cases. Large microscopic sections from these gross specimens were stained with various stains, except in 2 cases, in which I could not obtain the gross sections and had to be content with routinely cut and stained sections.

The microscopic criteria in some of these sections led me, an inexperienced observer, to doubt the accuracy of the first or primary pathological report. Therefore, because of this doubt, or because the original pathological report was at variance with the roentgenological diagnosis, some of these sections were presented to other pathologists and the variation in the reports submitted by them led to the investigation herein reported.

Eight microscopic sections were selected out of 69 consecutive surgical and autopsy specimens. I fully realize that 8 microscopic sections are not sufficient to settle the problem under consideration, but I doubt if one could get this number of representative pathologists to study a large number of sections, and I doubt if you would wade through this material if it were more extensive than that which is being presented to you.

An incomprehensible diversion of pathological opinion was encountered.

Pathologists who saw these sections and particularly internists and surgeons who have discussed this subject continually refer to these 8 sections as rare specimens selected from hundreds of cases during a long period of time. They often intimate, but rarely say, that these sections have been collected by a destructive critic. This erroneous conclusion concerning these being highly selected sections has become so prevalent that to dispel it I am giving the number, initial, and date of all of these sections in tabulated form.

The 8 microscopic sections were selected from specimens obtained between October, 1927, and October, 1932, and, as you will see, there are only 51 gastric lesions from which these 8 sections have been selected, so you can readily recognize that these are not highly selected microscopic sections. A re-examination of the sections made between those dates and other microscopic sections included in Table I collected after October, 1932, or with an earlier date reveals that there are many more controversial cases in this complete list of 87 cases. The clinical, roentgenological, or surgical diagnosis is not available on some of these additional sections and the additional sections were not presented to the group of pathologists, but from my observations I believe some of them would be even more controversial than some of those presented to

ductions of the identical roentgenograms in Fig. 2 A through H and see that you can now make a diagnosis of a gastric lesion and separate the cancers from the ulcers as readily as you can separate the red cards from the black in a playing deck. Yet, at that time and in fact long after that, roentgenography was considered worthless as a means to gastro-intestinal diagnosis. Every new pack has a joker, look out for the x-ray joker!

Fig. 3. Microscopic findings are so classical that in the majority of cases of gastric cancer the pathological diagnosis is easy and accurate, but there are also pathological jokers. It is easier for you to make a definite diagnosis on the roentgenograms in Figure 2 than on the photomicrographs in Figure 3.

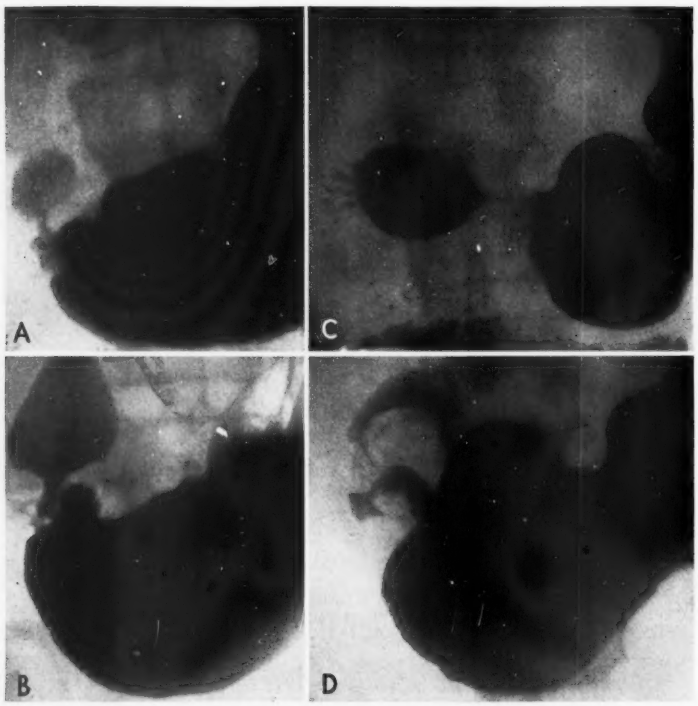


Fig. 4. A, As we now with afterthought review the roentgenological findings in these four series of films I believe that we should have made a positive diagnosis of carcinoma at the period of the first examination on the following findings:

(1) The crater is down pretty well toward the midline between the greater and lesser curvatures; (2) the induration distal to the crater protrudes into the cap causing a half density in the cap; (3) there is a definite irregularity on the greater curvature adjacent to the crater. B, The examination made August 27, 1931, a little more than a year later, with the crater essentially the size that it was originally even though it had apparently diminished in size in the meantime, with pressure on the cap and deformity of the greater curvature, makes us very suspicious of malignancy but should have led to a definite diagnosis of malignancy. C, The roentgenogram made October 5, 1931, shows that the growth of the cancer has eliminated the crater characteristics. D, In the roentgenogram made December 3, 1932, there is a definite annular growth causing an obstruction with the growth protruding or pushing the pyloric valve into the cap.

I am sure that those of you who know anything about roentgenography at all will now agree with me that this was manifestly malignant to such an extent that it is difficult for me to conceive how there was any doubt in my mind as to the question of malignancy.

these pathologists. These additional sections are indicated in the table by a question mark without a case number. Those with a question mark and a roman case number refer to the following 8 sections.

In reading the following case reports think of each one as your own case: if a clinician think of it from the clinical viewpoint; if a roentgenologist from this standpoint; if a surgeon from the surgical aspect as to indications for additional surgery or radiation therapy; if a pathologist you, too, might wish to try your luck on these sections.

The first of these cases to be reported was not in reality our first case but the one which led me to present this material in its present form and to select the title "Pathological Yardstick."

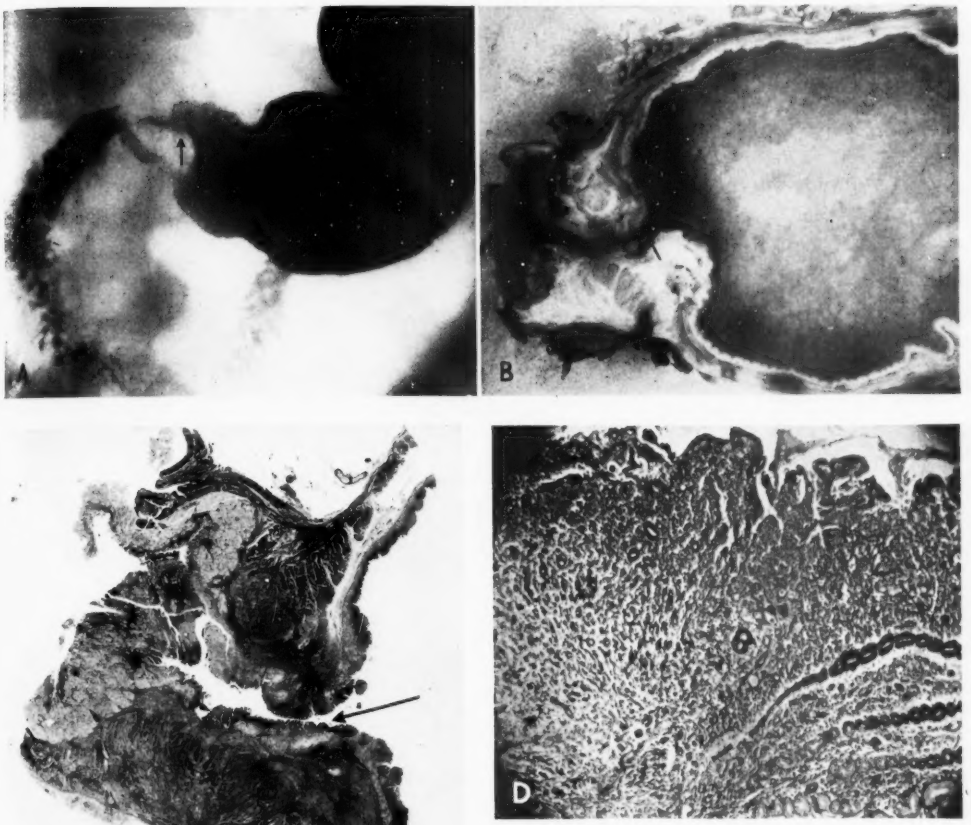


Fig. 5. This series of four figures, A, B, C, D (Case I, Dr. S., referred by Dr. Evan Evans; operated by Dr. John Erdmann) shows the correlation of the roentgenological, surgical, and microscopic findings. The clinical history was suggestive of gall-bladder disease. The roentgenological diagnosis was positive, carcinoma. The surgical finding was equivocal (small indurated area). Pathological diagnosis: negative, cancer; positive, duodenal ulcer with cicatricial connective tissue.

A, Roentgenogram with a positive diagnosis of a small cancer confirmed by many other serial films. B, The inside of the gross specimen which has been especially prepared by filling it with low-melting-point paraffin. (Compare the mass at the pylorus with the roentgenological findings.) C, A magnified photograph of the microscopic section. This should be compared with both the gross specimen and the roentgenogram. The arrow in each indicates the region from which the medium-power photomicrograph was made. The irregularity at this point is shown in the roentgenogram, the gross specimen, and the microscopic section. D, Photomicrograph of the diseased mucosa in the center of the lesion at the point indicated by the arrow.

Case I. The patient, Dr. S., was referred to me by Dr. Evan Evans with the request that I make an X-ray examination, give the diagnosis directly to the patient, and advise him whether he should be treated medically or surgically. This unusual procedure shifted onto my shoulders a great responsibility, and therefore I was perhaps flattered and unduly cautious at the time of the first examination on which I made a positive diagnosis of an organic lesion involving the pyloric end of the stomach, instead of carcinoma, and advised waiting 3 weeks, having an X-ray examination made each week to

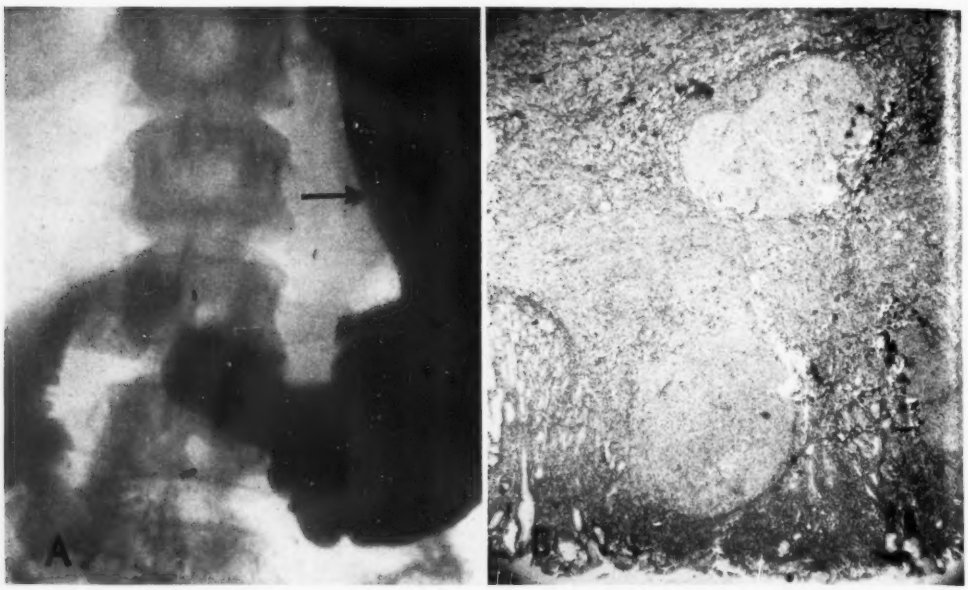


Fig. 6. Case II, Mrs. M. W. The clinical history indicated the presence of gastric ulcer. X-ray diagnosis was large ulcer, probably malignant. The surgical findings were a large ulcer with induration. Pathological diagnosis: sarcoma.

A, Roentgenogram showing a large ulcer surrounded by an immense area of induration that extends nearly up to the esophageal orifice. The point of its proximal limitation is indicated by an arrow. Also note the irregularity of the crater. The roentgen examination was equivocal (between cancer and ulcer), although it favored cancer. B, Photomicrograph of a routinely cut microscopic section. This section was obtained before I began to prepare gross specimens by the special method of filling the specimen with wax.

determine whether the lesion was progressing or retrogressing. At the end of the second examination, 1 week after the first (Fig. 5A) the lesion had not diminished in size but apparently it had not increased. But the findings were a little more clear cut and led me to advise immediate pylorectomy for gastric cancer. The patient consulted Dr. Erdmann, who, on his own clinical history, made a positive diagnosis of gall-bladder disease. The clinical history as obtained by both of us very strongly suggested gall-bladder disease; certainly there was nothing in it to justify a clinical diagnosis of gastric cancer.

On the roentgenological evidence Erdmann hesitated to advise the removal of the pylorus but the patient wanted it and I shared the responsibility, and a few days later Erdmann did a pylorectomy. The specimen was specially prepared by filling it with wax to prevent distortion during fixation and a photograph was made of the inside of the gross specimen showing the lesion as it involved both the greater and lesser curvatures (Fig. 5B). A complete section along the entire greater curvature, including the tumor mass observed in this photograph, was sent to the pathologist at the hospital in which the operation was performed but the pathologist did not see the entire gross specimen. Neither did he know of the controversy regarding the x-ray and clinical and surgical diagnoses. The routine pathological report was negative for gastric cancer, and a positive diagnosis of cicatricial connective tissue incident to a healed duodenal ulcer was made. Again the roentgenological diagnosis was proved wrong; this time by the *final yardstick of microscopic examination* based on the study of an adequate section extending through the entire length of the lesion and including normal tissue both proximally and distally. This negative diagnosis of cancer based on a microscopic examination, certainly was a shock to me considering the responsibility which I had assumed in advising the pylorectomy. If I had first consulted Pappenheimer, Konzelmann, Martland, McWhorter, and another pathologist who saw this specimen and made a negative diagnosis of cancer, thus sustaining the opinion of the original pathologist, my consternations would have been unbounded for having had the pyloric end of the stomach removed almost solely on the roentgenological diagnosis.

However, having learned not to be content with one pathological report, or even several when they are at variance with the clinical, roentgenological,

or surgical findings, I first submitted *my* section (see Fig. 5C) to Drs. Ewing, Stewart, and Stout. This section had been taken from the tissue adjacent to that examined by the first pathologist. A pathological report of gastric cancer was given by them on this section and the attending pathologist at the institution where the operation had been performed concurred with them when he examined my section but contended that there were no evidences of cancer in that microscopic section which had been examined at the hospital, an incident which he said frequently occurred, namely, carcinoma being observed in one region and not in another. Then he reviewed his section which was observed to be identical even to including the same groups of cells and he reversed the previous diagnosis which his associate had made of healed duodenal ulcer with cicatrization of connective tissue and gave a *positive diagnosis of gastric carcinoma.*

Both the original microscopic section and my own section were subsequently submitted to 19 pathologists who gave the following reports:

NON-MALIGNANT

Original pathologist, chronic duodenal ulcer
Pappenheimer, ulcer phagocytic cells
Konzelmann, chronic inflammatory
Martland, chronic ulcer
McWhorter, inflammatory lesion

MALIGNANT

Ewing, carcinoma
Second pathologist, carcinoma
Stout, carcinoma—undifferentiated colloid
Rhea, carcinoma—diffuse cell type
Mallory, carcinoma—colloid
Parker, carcinoma – colloid
Stewart, carcinoma — signet ring
Klemperer, carcinoma—scirrhus with mucus
Robinson, carcinoma — scirrhus
Pritchard, carcinoma — scirrhus
Foot, adenocarcinoma — colloid type
Gray, adenocarcinoma—mucoid
Geschickter, linitis plastica; signet ring
Masson, linitis plastica
Simard, carcinoma — linitis plastica

NON-MALIGNANT

ORIGINAL PATHOLOGIST. *Non-malignant*—chronic duodenal ulcer. Old cicatricial connective tissue; infiltrating Brunner's glands No evidence of cancer.

PAPPENHEIMER. *Non-malignant*—I do not believe it to be carcinoma. *Criteria*—(A) Appearance is unusual because of the presence of numerous mucin containing cells in the stroma. These I regard as phagocytic cells rather than carcinoma cells. (B) Cells do not appear to invade the deeper tissues.

KONZELMANN. *Non-malignant*—chronic inflammatory lesion *Criteria*—Not given.

MARTLAND. *Non-malignant*—chronic ulcer. No cancer. *Criteria*—Not given.

MCWHORTER. *Non-malignant*—Probably inflammatory lesion *Criteria*—See no evidence of tumor growth.

MALIGNANT

EWING. *Malignant*—carcinoma. Did not specify type of carcinoma or actual criteria on which he based diagnosis.

SECOND PATHOLOGIST. *Malignant*—carcinoma.

STOUT. *Malignant*—carcinoma, undifferentiated colloid type. *Criteria*—(A) Infiltrative growth of "signet ring" cells; (B) other atypical isolated hyperchromatic tumor-like cells.

RHEA. *Malignant*—carcinoma; diffuse cell type. *Criteria*—Mucus? Suggest mucicarmine stain.

MALLORY. *Malignant*—colloid carcinoma, very scirrhus in places. *Criteria*—Not given.

PARKER. *Malignant*—colloid carcinoma, very scirrhus in places. *Criteria*—Not given.

STEWART. *Malignant*—carcinoma—"signet ring" type. *Criteria*—Not given.

KLEMPERER. *Malignant*—scirrhus with mucus. *Criteria*—Notes mislaid.

ROBINSON. *Malignant*—scirrhus carcinoma. *Criteria*—Loss of glandular elements and replacement by sheets of large cells which vary in size and shape and staining characteristics. Some have large hyperchromatic nuclei, others pale vesicular ones. These cells with some modifications are infiltrating the muscle coat.

PRITCHARD. *Malignant*—scirrhus carcinoma. Marked fibrosis of deeper layers of mucosa, muscularis mucosa, submucosa and muscularis. Great thickening of submucosa. *Criteria*—There is a diffuse lymphocytic infiltration with few nodules. Scattered throughout are small polyhedral cells with hyperchromatic nuclei. No extra gastric lymph nodes in section. These cells I consider epithelial. They appear to originate in the tip of the glands.

FOOT. *Malignant*—adenocarcinoma of colloid or mucus producing type; Brunner gland region suggested. *Criteria*—(A) Anaplastic cells arranged in acinoid fashion or discreetly; (B) mitotic figures present; (C) "signet ring" cells; (D) marked invasion of the wall.

GRAY. *Malignant*—mucoid adenocarcinoma. *Criteria*—(A) Diffuse, anaplastic growth of mucus producing glands, involving mucosa and submucosa. (B) Pleomorphic cells; the nuclei and nucleoli are hyperchromatic; and mitotic forms are present. (C) In some areas the nuclei are quite widely separated by mucoid substances.

GESCHICKTER. *Malignant*—linitis plastica; "signet ring" cells. *Criteria*—Not given.

MASSON. *Malignant*—linitis plastica. *Criteria*—Cancerous mucous cells throughout; hyperproduction of sclerosis.

SIMARD. *Malignant*—atypical epithelium; form linitis plastica. Carcinoma diffuse form. *Criteria*—(A) Oil immersion cells with light protoplasm, vacuolar nucleus pushed aside—mucus?; (B) diffuse infiltration of cells into submucosa, the muscular layers, the peritoneum; (C) desire mucicarcmine for mucus. Fixation poor.

The x-ray diagnosis of gastric carcinoma and clinical diagnosis of gall-bladder disease were both proved wrong by the *primary* pathological report of simple duodenal ulcer, *no cancer*. Such a primary pathological report would be used for surgical statistics, business arrangements, life insurancce, etc. Father Time took the patient in 14 months with his carcinomatous reaper.

The preponderance of pathological opinion is three to one in favor of malignancy but as we shall see in subsequent cases the preponderance of opinion is not always in accord with the dictum of Father Time.

CASE II. Mrs. M. W., referred by Dr. Blank, operated upon by Dr. Blank, was admitted to French Hospital on March 6, 1924, with clinical diagnosis of ulcer; roentgen films made elsewhere showed a small ulcer on the lesser curvature. This ulcer was removed by V resection but the symptoms persisted—in fact were aggravated. About 1 month later we made an x-ray examination (Fig. 6A) and reported as follows: "I believe we are justified in making a positive diagnosis of a large indurated area on the lesser curvature with an ulcerated center. This may be a large simple ulcer or a malignancy, but the weight of the evidence is in favor of its being malignant."

On the basis of this roentgen report a partial gastric resection was performed by Dr. Blank by Bill-

roth II procedure. From a study of the films it is evident that it would have been almost impossible to have removed the stomach above the proximal edge of the induration. The patient's symptoms continued and an x-ray examination on June 16, 1924, showed marked obstruction and 24 hour retention due to closure of the gastro-intestinal stoma. At that time I was unable to detect any evidence of a tumor mass in the stomach obstructing the stoma. Subsequently Dr. Blank re-operated and did a gastro-enterostomy, carrying a long loop of jejunum to the remaining portion of the stomach.

The patient was finally discharged from the hospital on February 20, 1925, almost a year after her admission. During that time she had had three x-ray treatments of 5 minutes each with 140,000 kilovolts, and 3 millimeters of aluminum. This made a total of 15 milliampere minutes.

A microscopic examination of a section of the lesion (Fig. 6B) was made by Dr. McWhorter who recognized the findings as unusual and made the following pathological report: "Diagnosis of sarcoma of the stomach." He was sustained in this diagnosis by 6 other pathologist friends of his to whom he rather informally showed this section. A short time later Dr. Ewing was in consultation on another case at the hospital, and I asked him if he wanted to see a sarcoma of the stomach. Thinking that I referred to the x-ray, he exclaimed: "Yes, I certainly do!" He was surprised when we brought him the microscopic sections and then he said—"No, this isn't sarcoma. This is carcinoma, undifferentiated and very malignant."

With these two divergent opinions as to the type of the lesion, the section which had been examined by Ewing was presented to Pappenheimer, who, during a cursory examination looked at the section, and said that it was a granuloma, non-malignant, and handed the slide back to me. A smile, or some other look on my face led him to inquire "why" and I told him Dr. Ewing had seen this section and had made a diagnosis of cancer, which prompted him to grab the slide and look at it again, at which time he said he was going to retract his hasty opinion and that the slide wasn't good enough to justify a diagnosis. Pappenheimer then asked me to get the block from Dr. McWhorter and he had his technician cut and stain several sections. He was as yet unwilling to make a diagnosis because the block was improperly mounted, so he remounted the block and made additional sections (Fig. 6B) and made a diagnosis of *carcinoma*, undifferentiated and very malignant; thus confirming Ewing's diagnosis, which he knew. This difference of opinion regarding the type of lesion and the unusual appearance caused me to include this microscopic section among those which were subsequently presented to all the pathologists on this list, all of whom saw this particular section. Opinion was almost unanimous that the lesion was malignant. Only one pathologist, Konzelmann of Temple, made a definite diagnosis of non-malignancy. Lacassagne of Paris did not commit himself as to malignancy or non-malignancy, but he suspected it was not malignant; nor did he commit himself to an opinion as to the type of lesion. Of the twenty-two who maintained that it was definitely malignant there was a wide variation of opinion as to the type of lesion.

NON-MALIGNANT	
Konzelmann, chronic inflammatory	Gray, carcinoma
Lacassagne, perhaps carcinoid	Rhea, carcinoma
Pappenheimer (?), granuloma (1st report)	Pritchard, carcinoma
MALIGNANT	Klemperer, sarcoma
Ewing, carcinoma, undifferentiated	Bell, sarcoma
Stewart, solid carcinoma	Robinson, sarcoma
Bertrand, carcinoma	Mallory, sarcoma
Aschner, carcinoma	Parker, sarcoma
Foot, carcinoma	Broders, sarcoma
Jorstad, carcinoma	Masson, lymphosarcoma
Martland, malignant	Simard, lymphosarcoma
	McWhorter, lymphosarcoma
	Pappenheimer, carcinoma?
	Stout, carcinoma?

NON-MALIGNANT

KONZELMANN. *Non-malignant*—chronic inflammatory process, mucosa cut tangentially. *Criteria*—(A) No circumscribed tumor mass; (B) cells are divisible into 2 or 3 types, the individual characteristics of each type are fairly uniform; (C) no smaller nuclei and nucleoli; (D) proper proportion between nucleus and cytoplasm; (E) rare mitotic figures among epithelium-like cells; (F) no connective tissue reaction, such as one expects to find in an epithelial tumor; (G) many inflammatory cells.

LACASSAGNE. *Non-malignant* (difficult). Perhaps carcinoid (similar to carcinoid of appendix described by Masson). No metastases. Perhaps, but less likely, lympho-granulomatosis. *Criteria*—Not given.

PAPPENHEIMER. *Non-malignant*—in his first report said—"Granuloma." (?) *Criteria*—Not given. This was his first impression from a cursory examination of the section which he immediately withdrew.

MALIGNANT

EWING. *Malignant*—carcinoma; infiltrating. *Criteria*—diffuse growth of atypical cells infiltrating all tissues.

STEWART. *Malignant*—very malignant—solid carcinoma. *Criteria*—No further criteria.

BERTRAND. *Malignant*—very malignant—carcinoma. *Criteria*—Malignant cells together, invading the chorion, muscularis mucosa and submucous membrane.

ASCHNER. *Malignant*—carcinoma. *Criteria*—Spheroidal cells.

FOOT. *Malignant*—acute diffuse carcinoma. *Criteria*—Normal topography replaced by rapidly growing, wildly disordered, epithelial cells, showing anaplasia, mitoses, hyperchromasia and dissociation.

JORSTAD. *Malignant*—carcinoma, for the most part undifferentiated; adenocarcinoma (Grade 4). *Criteria*—(A) Certain areas throughout muscularis differentiated to gland formation; (B) cells are hyperchromatic; (C) there is no invasion throughout the normal tissue; (D) stroma is that seen in epithelial structures.

MARTLAND. *Malignant*—enormous infiltration of tumor cells, mitosis, etc. Section too faded to diagnose type.

GRAY. *Malignant*—undifferentiated small cell carcinoma. *Criteria*—(A) Growth extremely cellular with minimal amount of fibrous stroma; (B) cells are spheroid with ill defined cytoplasm; (C) vascularity not marked; (D) some mitosis.

RHEA. *Malignant*—small cell diffuse carcinoma. Section poor. Ulcer secondary malignancy at one margin. *Criteria*—Not given.

PRITCHARD. *Malignant*—small cell diffuse carcinoma. *Criteria*—Cell type, arrangement and infiltration.

SARCOMA

KLEMPERER. *Malignant*—sarcoma (reticulum cell, so called lymphosarcoma) moderately malignant; some cases well even 4 years after operation. *Criteria*—(A) Diffuse infiltration of entire

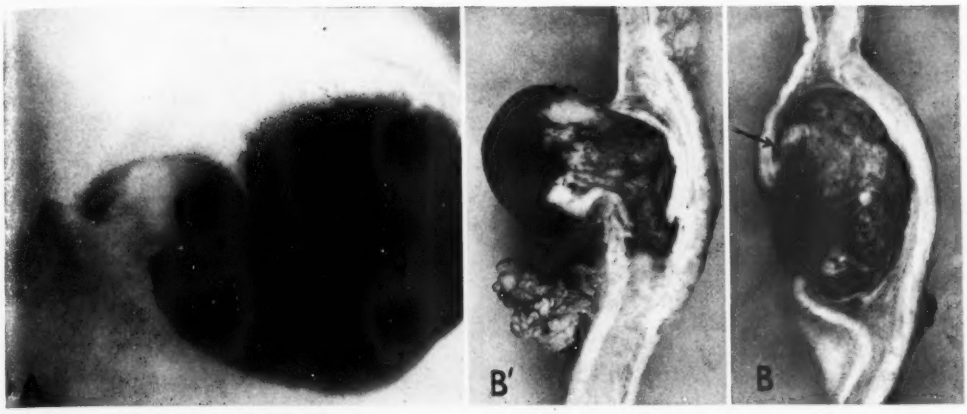


Fig. 7. Case III. Mr. G. B., operated upon by Dr. Kingsley Roberts. The clinical diagnosis was cancer; roentgenological diagnosis, cancer, but should have been neoplasm on the roentgenological findings we studied; surgical findings, carcinoma; pathological diagnosis, atypical gastric carcinoma.

A, Roentgenogram showing the spherical tumor on the greater curvature near the pylorus with superficial ulceration. B′, Photograph of a gross subsection of a sleeve resection. This specimen could not be filled with paraffin. Part of the tumor mass projects into the lumen of the stomach and is ulcerating into the stomach. B, Part of the tumor projects into the peritoneal cavity. A small crater shown in the roentgenogram corresponds with the ulcerating area in the neoplasm. C, Medium-power photomicrograph of a region shown at the arrow in B.

wall; (B) type of cell stellate with large plate nucleus; (C) blood count desired, though I do not think it is a leucemic condition.

BELL. *Malignant*—sarcoma. *Criteria*—Round cell sarcoma; another possibility leucemic infiltration.

ROBINSON. *Malignant*—retithelioma (reticular cell sarcoma). *Criteria*—(A) Tumor cells round to oval in shape; (B) pale staining reticulated nuclei with appreciable amounts of pink staining cytoplasm; (C) in places cells are growing in a somewhat follicular manner, in other areas as sheets and whirls.

MALLORY. *Malignant*—reticulum cell sarcoma. *Criteria*—Not given.

PARKER. *Malignant*—reticulum cell sarcoma. *Criteria*—Not given.

MALIGNANT

BRODERS. *Malignant*—odd lesion for stomach; not a carcinoma; sarcoma probably; lympho type. *Criteria*—Not given.

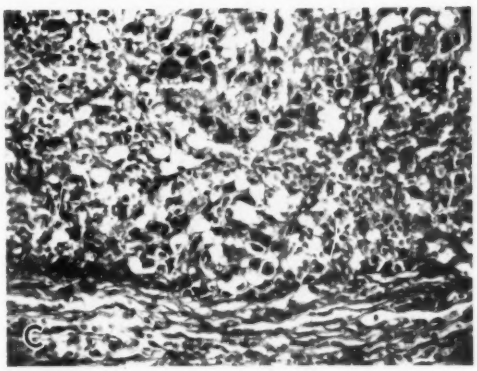
MASSON. *Malignant*—lymphosarcoma. *Criteria*—Diffuse infiltration of mucosa, submucosa, and muscle layers by round cells.

SIMARD. *Malignant*—histologically malignant—lymphoblastoma? *Criteria*—Diffuse infiltration of muscular layers; very poor section—above statement impression only.

MCWHORTER. *Malignant*—probably malignant—mildly; sarcoma: lympho type. *Criteria*—Have seen too few of these to know anything about the follow-up.

MALIGNANT QUESTIONABLE

PAPPENHEIMER. *Very malignant*—carcinoma—undifferentiated malignant; (6 years later—lymphosarcoma). *Criteria*—Not given at first examination. Recent study (6 years later of same section, section faded in meantime). "I cannot make a positive diagnosis but am inclined to regard tumor as lymphosarcoma because of diffuse infiltration without destruction of epithelium."



STOUT. *Malignant*—neoplasm. Sarcoma or undifferentiated carcinoma, probably sarcoma. *Criteria*—(A) Infiltrative growth; (B) many mitoses; (C) no secretion of mucin or differentiation into glands; (D) possibly reticulum cell sarcoma from reticulum of stomach lymphoid tissue.

The clinical and x-ray diagnoses were equivocal. We did not know whether the lesion was malignant or not. *But* measured by the pathological yardstick (by 23 out of 24 pathologists) it was malignant, viciously malignant. The x-ray man could not be expected to see the cancer cells or tell whether the ulcer was malignant or benign. The patient is alive and well at 12 years.

The tremendous preponderance of opinion in favor of malignancy, even though there was great diversity as to the type of lesion, reminds me a little of the admiring mother who said that everybody was out of step except Johnny. In this case Johnny was Konzelmann, who elaborated his criteria more

than all others; he knew his left footstep was on the impulse beat of the music.

CASE III. Mr. G. B., admitted to the Fifth Avenue Hospital in June, 1931. Patient of Dr. Kingsley Roberts. Following is an excerpt from the roentgen report: "After a barium meal there is evidence of a tumor mass in the pyloric end of the stomach near the pylorus (Fig. 7A). This is located in the region of the greater curvature. There is evidence of a crater in the center or near the center of the mass. The tumor mass is somewhat circular in shape and presses into the lumen of the stomach when the patient is in the prone position. I believe that the weight of the evidence is in favor of this being a carcinoma." Present review of the report when writing this: The only evidence in this report of its being an x-ray joker is the wording in the first clause—"A tumor mass"—also the next to the last clause should read—"according to the doctrine of chance this should be carcinoma but the x-ray criteria is in favor of its being something else, at least an x-ray joker."

A pyloric resection by Dr. Roberts revealed a gross lesion (Fig. 7B) that was as unusual as the roentgenological findings. The gross specimen viewed from within (Fig. 7B′) and also on cut section showed findings almost identical with the x-ray findings. A large, adequate, well stained section (see Fig. 7C) was considered non-malignant by Konzelmann and malignant by all the rest of the pathologists.

Their findings are as follows:—

NON-MALIGNANT	
Konzelmann, acute ulcer	Pritchard, myosarcoma
	Stewart, sarcoma
MALIGNANT	Rhea, sarcoma
Mallory, carcinoma	Robinson, leiomyosarcoma
Masson, carcinoma	Pappenheimer, sarcoma
Geschickter, carcinoma	Foot, leiomyosarcoma
Parker, carcinoma	Klemperer, probably malignant
Martland, carcinoma	
Gray, carcinoma	McWhorter, probably malignant
Ewing, sarcoma	Simard, no opinion

NON-MALIGNANT

KONZELMANN. *Non-malignant*—acute ulcer. *Criteria*—(A) Organizing blood clot; (B) cells in clot as proliferating fibroblasts; C) few histocytes

MALIGNANT—CARCINOMA

MALLORY. *Malignant*—carcinoma; edematous. *Criteria*—metastasis to lymph node.

MASSON. *Malignant*—carcinoma; probably mucus secreting. *Criteria*—invading secondarily and ulcerating the mucosa—probably arising from an embryonic remnant in the muscular layers.

GESCHICKTER. *Malignant*—carcinoma. *Criteria*—(A) Diffuse proliferation of cells with large nuclei; (B) hemorrhage and necrosis as in malignancy; (C) indefinite formation; variation in chromatin.

PARKER. *Malignant*—carcinoma; edematous. *Criteria*—Metastasis to lymph node.

MARTLAND. *Malignant*—colloid carcinoma. *Criteria*—Extension into the serosa.

GRAY. *Malignant*—metastatic carcinoma. *Criteria*—(A) There are two encapsulated growths, one within submucosa, one attached to the serosa; (B) growth is composed of polyhedral cells with clear cytoplasm and deep-staining epithelial nuclei; (C) necrosis is prominent throughout; (D) giant cell formation with cells containing 2 to 4 nuclei is marked; (E) vascularity is marked and interstitial hemorrhage is present; (F) in certain areas the cord and column-like distribution together with character of cytoplasm suggest adrenal origin.

MALIGNANT—SARCOMA

EWING. *Malignant*—sarcoma. "Yes. Angiomyoma. *Criteria*—No evidence of epithelial origin; on all sides of the tumor one finds muscle. This is an impression, opinion. One cannot give—(he did not finish the sentence). This is a funny one—old atrophic gastritis of mucosa; runs off into a hypertrophic gastritis. Very unusual—very peculiar thing; never saw anything like this. This patient ought to have gotten well—did he?"

PRITCHARD. *Malignant*—myosarcoma or liposarcoma. *Criteria*—(A) Cell type and extension via lymphatics into omentum; (B) fat stains-polarize-phosphotungstic stain; (C) no myofibrils or stria can be made out in HOE stain.

STEWART. *Malignant*—sarcoma, probably of muscle (myosarcoma). *Criteria*—Largely anatomical. Tumor except where ulcerated is surrounded by muscle and shows a curious delimitation by muscle. Large multinuclear cells in spindle form and reticular arrangement.

RHEA. *Malignant*—sarcoma—probably smooth muscle. *Criteria*—(A) Encapsulated tumor composed of large irregular cells; (B) extension via lymphatic to serosa.

ROBINSON. *Malignant*—leiomyosarcoma. *Criteria*—(A) Made up of atypical spindle shaped cells which have considerable cytoplasm, large reticulated nuclei; (B) growth fairly well circumscribed; (C) a secondary appears in an adjacent gland.

PAPPENHEIMER. *Malignant*—some type of sarcoma, possibly leiosarcoma. I am doubtful whether it is primary in the stomach. *Criteria*—Malignant, because of attached lymph node being completely invaded.

FOOT. *Malignant*—leiomyosarcoma. *Criteria*—Large anaplastic, hyperchromatic cells with mitoses arranged anatomically in cords or sheets suggesting embryonal smooth muscle. They possess primitive sheaths and form numerous giant cells. Widespread infiltration of wall. Metastasis to lymph node. Tumor lies in inner muscular coat.

EQUIVOCAL

KLEMPERER. *Malignant*—probably. *Criteria*—Not given.

MCWHORTER. Unfamiliar. Would consider this type probably malignant, rather than metastatic. *Criteria*—Not given.

SIMARD. Poorly fixed and stained; cannot commit myself on this section.

Clinical and x-ray diagnosis equivocal. Measured by the pathological yardstick, the type of lesion is still equivocal—he should be dead of malignancy but he is alive and husky at 6 years.

Ewing and Stewart the first time they saw this section both temporarily avoided committing themselves concerning the type of lesion but later they both described it in detail as given above.

There is a preponderance of opinion in favor of malignancy or at least neoplasm, equally divided into carcinoma or sarcoma.

CASE IV. Mr. J. C. In this case the incident associated with the roentgenological examination is similar to the first; viz.: the microscopic examination indicated the x-ray was wrong. The examination (Fig. 8A) showed a definite lesion on the lesser curvature of the stomach about which there was a difference of opinion among those of us who were

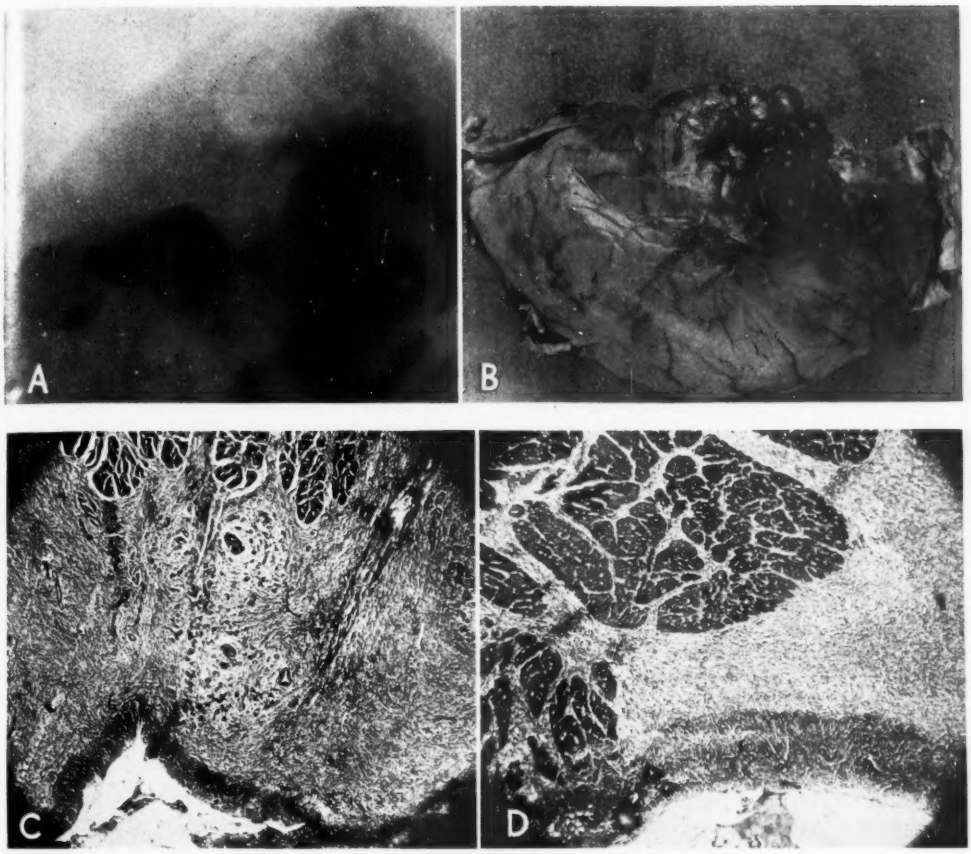


Fig. 8. Case IV, Mr. J. C., operated upon by Dr. Frederick Bancroft. The clinical diagnosis was ulcer; roentgenological diagnosis, cancer; surgical findings, ulcer; pathological report, simple benign ulcer, in spite of pressure being brought to have the pathologist change it.

A, Roentgenogram showing lesion near the sulcus angularis with a superficial area of ulceration and a large area of induration. B, Photograph of the outside of the specimen showing the peculiar tumor resembling a bunch of grapes. C, Photomicrograph from the distal half of the ulcer bed showing a definite orthodox evidence of the presence of cancer. D, Photomicrograph of the proximal half of the ulcer showing that there is no orthodox evidence of cancer.

associated in our practice of roentgenology. The report of the x-ray examination is as follows:

Roentgenograms of the gastro-intestinal tract immediately and 6 hours after a barium meal show an indurated lesion on the lesser curvature of the stomach and the pyloric end of the stomach just distal to the sulcus. It is about 2 inches proximal to the pylorus. There is no definite crater that can be shown at this time. There is an indentation on the greater curvature surface opposite this lesion. This area is fixed and in the present films the proximal portion of the stomach overrides and obscures the area. We believe that this is an infiltrative lesion involving the lesser curvature surface in the region described. It is either the result of a former gastric ulcer with fixation and adhesions or malignancy. The weight of the evidence is in favor of malignancy. The pylorus is in a state of contraction and we believe that this area is also fixed from some irritation or some former process. There is no obstruction.

One of us (L. G. C.) stood out for a diagnosis of carcinoma while others were unwilling to go further than a diagnosis of an organic lesion of a neoplastic type. The patient was operated on by Dr. Bancroft and at the time of the exploration the lesion observed roentgenologically was readily detected. Dr. Bancroft considered its external appearance unusual and, on palpation, the lesion did not have the stony hardness considered characteristic of a carcinoma. A partial gastric resection was done; and the specimen prepared in a special manner by filling it with low-melting point paraffin. It was then cut longitudinally through the center of the crater (Fig. 8B). I retained ½, the attending pathologist, Dr. Jessup, took the other.

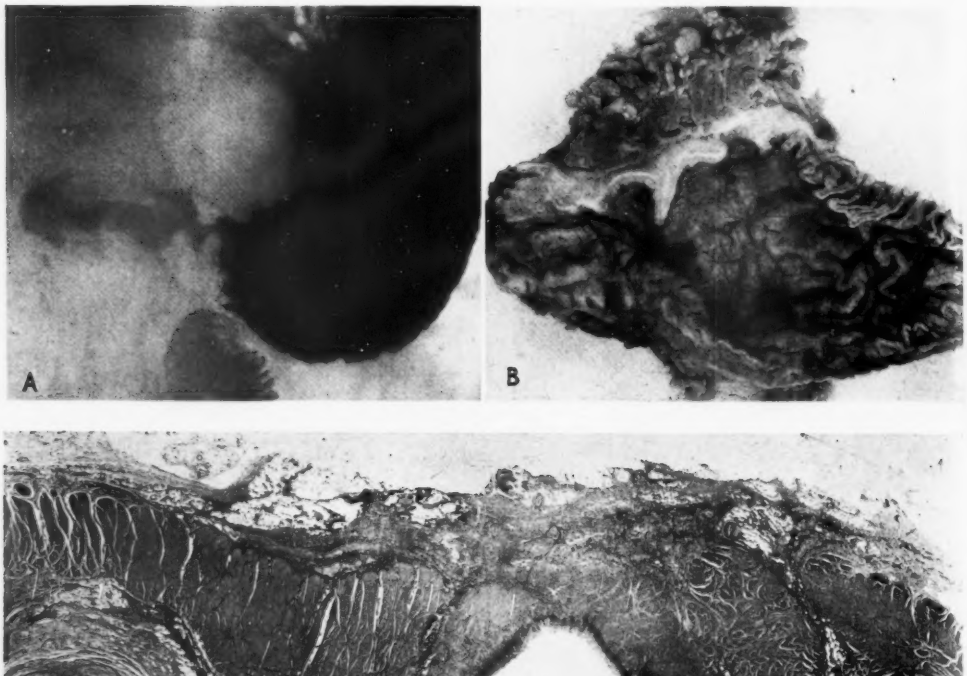
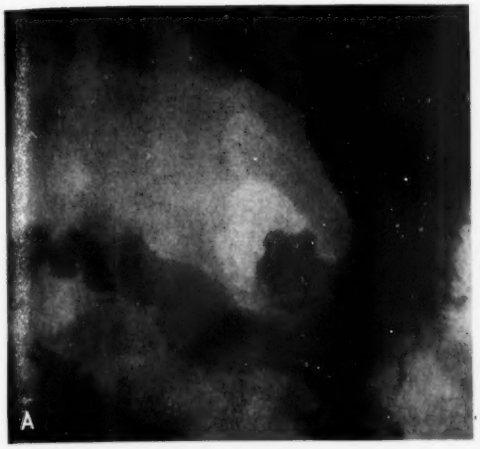


Fig. 9. Case VI, Mr. A. W. The clinical diagnosis was gastric ulcer; the roentgenological diagnosis, gastric ulcer; the surgical findings, gastric ulcer; the pathological diagnosis, gastric ulcer.

A, A multiple ulcer with marked deformity of the pyloric end of the stomach. Such gross deformity with such slight ulceration should have made us suspicious of this not being a simple ulcer. B, Photograph of the inside of the specimen showing multiple ulcers and gross deformity corresponding with the roentgenological findings. Note the small area on the lesser curvature shown in greater detail in C. C, Magnified photograph of the microscopic section showing the architectural characteristics of the lesion, especially the relation of the crater to the various coats. Although there was practically no pathological controversy in connection with this case, it is my opinion that this section is the most important of all those presented in this article.

Considering that there was some controversy concerning the clinical, roentgenological, and surgical findings, a large section including the crater and the indurated area proximal and distal to the crater was included in both his microscopic sections and those which I subsequently had mounted and stained. The pathological report given by Dr. Jessup was simple benign ulcer, no evidence of malignancy, and from this diagnosis he could not be budged in spite of an overwhelming effort on the part of some of us to convince him that a certain group of cells in the base of the ulcer were malignant. X-ray diagnosis,



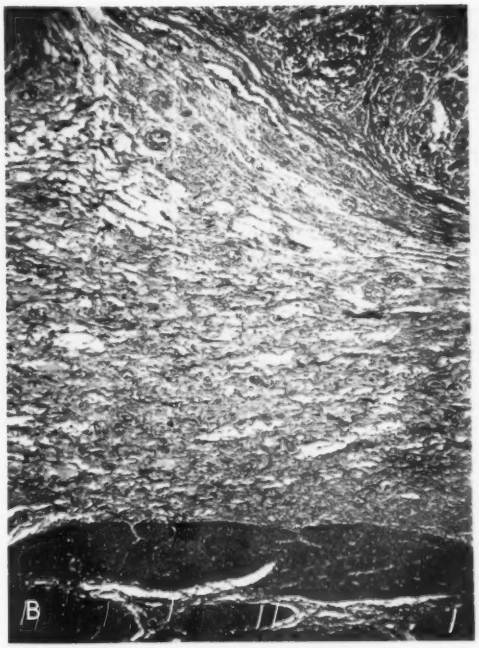


Fig. 10. Case VII, Mrs. D, operated upon by Dr. Kingsley Roberts. The clinical diagnosis was gastric ulcer; the roentgenological diagnosis, gastric ulcer, not a simple type; surgical findings, gastric ulcer; pathological diagnosis, gastric ulcer. The sections submitted to the pathologist were not at the crater but included the submucosa on the greater curvature which shows tremendously thickened and infiltrated tissue.

A, Roentgenogram showing a large ulcer on the lesser curvature with irregular crater and extreme irregularity of the mucosal pattern on the greater curvature from which region the microscopic section was removed. B, Photomicrograph showing submucosa thickened and infiltrated. The circular muscle coat is at the bottom of the illustration. The muscularis mucosa and base of the submucosa is at the top. The type of tissue in the submucosa was the pathological question under consideration.

gastric cancer (L.G.C.) clinical and surgical diagnosis equivocal. Primary pathological report, simple ulcer, no cancer. I was wrong as measured by the primary pathological yardstick—but 24 other pathologists all said it was malignant. Their diagnosis did not go on the chart. The man applied for life insurance and the only pathological report said it was not cancer. I don't know if he got it. When this section was presented to Ewing and Stewart, Jessup was supported by both, according to reports signed or initialled by each of them. The lesion (as shown in Figure 8C) was considered malignant and the type carcinoma by all other observers. The fact that 21 of these 24 men considered this lesion either definitely malignant or suspiciously malignant, is of special significance, particularly when associated with our subsequent consideration of types of ulcers which are malignant or tend to become malignant.

In discussing this initialled report, Ewing brought out at our co-ordinating conference a fact that is well worth consideration and therefore will be herein elaborated upon more than it seemingly deserves. Ewing, in defense of his initialled report, stated that this slide must have been shown to him late in the afternoon or without his having given it careful consideration. Under these circumstances I fully appreciate that he should not be held responsible for this diagnosis because we well know one is frequently asked to give curbstone diagnosis—the pathologist on a microscopic section and the roentgenologist on someone else's x-rays and in most of these cases, be they sections or roentgenological findings they should be given the greatest attention because usually they are either pathological or roentgenological jokers. In this case, therefore, the sections were later presented to Ewing and Stewart at which time they gave them the most careful consideration and reported them an unmistakable cancer with definite well defined differentiated groups of epithelial cells well down in the bed of the ulcer.

NON-MALIGNANT

Jessup, simple benign ulcer
Ewing (?), benign ulcer; small area questionable
Stewart (?), ulcer with some atypical glands

MALIGNANT

Ewing (?), carcinoma
Stewart (?), carcinoma
Geschickter, carcinoma
Aschner, carcinoma
Bell, adenocarcinoma
Mallory, adenocarcinoma
Parker, adenocarcinoma
Foot, adenocarcinoma
Martland, adenocarcinoma
McWhorter, adenocarcinoma
Robinson, adenocarcinoma
Gray, adenocarcinoma
Lacassagne, adeno epithelioma
Konzelmann, adenocarcinoma
Bertrand, epithelioma
Stout, cancer on ulcer
Klemperer, cancer on ulcer
Pappenheimer, cancer on ulcer
Pritchard, cancer on ulcer
Rhea, cancer on ulcer
Masson, cancer on ulcer
Simard, cancer on ulcer

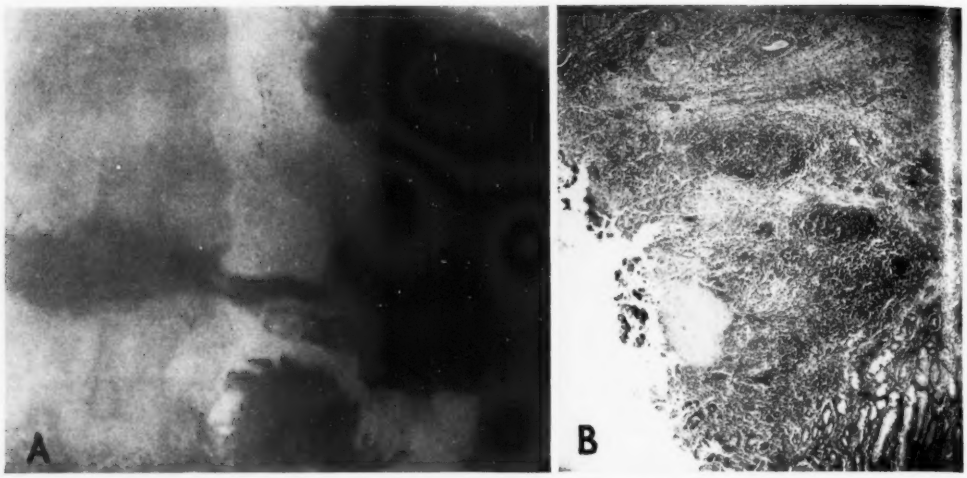


Fig. 11. Case VIII, Mr. P. S., referred by Dr. Andrews, operated upon by Dr. Eugene Pool. The clinical diagnosis was equivocal; roentgenological diagnosis, equivocal, one for and one against cancer. Two examinations were made, the second after a period of 1 year had elapsed. The surgical findings, gastric cancer; pathological report, simple ulcer. Later this was changed on some of the hospital records to sarcoma.

A, Roentgenogram showing large shallow crater with marked gross deformity that did not change materially between the two roentgen examinations made a year apart. The diagnosis at the first examination, probably malignant; at the second, probably non-malignant. B, Photomicrograph showing submucosa at the tip of the crater with the mucosa at the bottom of the section and the circular muscle coat at the top.

NON-MALIGNANT

JESSUP. *Non-malignant*—simple benign ulcer. *Criteria*—Not given.

EWING (?). *Non-malignant*—benign ulcer. Small area questionable. *Criteria*—Not given.

STEWART (?). *Non-malignant*—ulcer with some atypical glands. *Criteria*—Not given.

MALIGNANT

EWING (?). *Malignant*—carcinoma. *Criteria*—Not given.
STEWART (?). *Malignant*—carcinoma. *Criteria*—Not given.
GESCHICKTER. *Malignant*—cancer. *Criteria*—Not given.
ASCHNER. *Malignant*—carcinoma. *Criteria*—Not given.

ADENOCARCINOMA

BELL. *Malignant*—adenocarcinoma. *Criteria*—Not given.
MALLORY. *Malignant*—adenocarcinoma. *Criteria*—Not given.
PARKER. *Malignant*—adenocarcinoma. *Criteria*—Not given.
FOOT. *Malignant*—adenocarcinoma. *Criteria*—(A) Atypical glandular cells in floor of ulcer; (B) variation in size, shape and arrangement of cells; (C) irregular tubule production in most of cells; (D) irregular atypical mitosis.
MARTLAND. *Malignant*—adenocarcinoma. *Criteria*—Not given.
MCWHORTER. *Malignant*—adenocarcinoma. *Criteria*—Infiltration of submucosa and muscularis with glandular epithelioma.
ROBINSON. *Malignant*—adenocarcinoma. *Criteria*—Atypical cells infiltrating muscle and forming pseudogland acini. Appears to be developing in the margin of a chronic ulcer.
GRAY. *Malignant*—adenocarcinoma. *Criteria*—(A) There is the marginal inflammatory tissue of this ulcer, a circumscribed area of anaplastic glandular growth. Except for diffuse infiltrative growth the criteria for malignancy are present. There is loss of polarity, variation in size of cells, increased chromatic nuclear substance and mitosis; (B) there are lymphoid deposits; (C) as there is but slight reversion to embryonal type of cell, it would be classified as Grade 1. Whether or not a carcinoma *in situ* or a chronic ulcer of the stomach would not metastasize is the mooted question.
LACASSAGNE. *Malignant*—adenoepithelioma. *Criteria*—Not given.
KONZELMANN. *Malignant*—adenocarcinoma. *Criteria*—Atypical granules in floor of ulcer. Variation in size, shape and arrangement of cells. Irregular tubule production. Eosinophiles. Occasional atypical mitosis.
BERTRAND. *Malignant*—epithelioma. *Criteria*—Typical epithelioma with gland-like formation; basophilic protoplasm.

MALIGNANT—CANCER ON ULCER

STOUT. *Malignant*—carcinoma, at margin of a pre-existing ulcer. *Criteria*—Carcinoma is represented by an infiltrative growth of atypical glands.
KLEMPERER. *Malignant*—most probably cancer on basis of an ulcer. *Criteria*—Peculiar tubular type of carcinoma at one end suggests ulcer carcinoma.
PAPPENHEIMER. *Malignant*—chronic ulcer in which adenocarcinoma is developing at one end. *Criteria*—Signs of developing adenocarcinoma at one end furnish the criteria.
PRITCHARD. *Malignant*—adenocarcinoma commencing in the mucosa at margin of ulcer, extending back into submucosa and along lateral wall of ulcer into muscularis superimposed on chronic ulcer. *Criteria*—Not given.
RHEA. *Malignant*—carcinoma in mucosa at margin of ulcer extending back along the submucosa and along lateral wall of ulcer into muscularis. *Criteria*—Not given.
MASSON. *Malignant*—probably ulcerocancer diaphragm type. *Criteria*—Not given.
SIMARD. *Malignant*—ulcer and carcinoma. *Criteria*—If only one side of the ulcer has carcinoma it is cancerized ulcer. If not, a cancer in diaphragm or an ulcerating cancer or "ulcerocancer."

This section does not seem to be of interest except for the fact that the previous pathological diagnosis based on microscopic section indicated that the x-ray diagnosis was wrong and that diagnosis would have stood in

spite of efforts to get the pathologist to change it, if the section had not been presented to twenty-two other pathologists. But, when combined with the next section, it serves as a very important link in a chain of evidence on the criteria of growing tissue which is the subject of a second article soon to be presented.

The fifth microscopic section presented (Fig. 8D) was the other half of the same lesion as described in Case IV (Fig. 8 A,B,C). The ulcerating area and its surrounding area of induration was rather large for a single mounting and therefore it was cut in two directly through the center of the crater; half of the lesion being mounted on one slide and the other half on another slide.

In presenting this other half of the section, without the pathologists knowing it was the opposite half of the section they had seen before, I have been accused of trickery which has aroused more or less the ire of some of the pathologists. I can only say in sincerity that this was done, not with the object of tricking or catching them in the diagnosis, but it was done for 2 distinct reasons:

First, to demonstrate a fact well known among pathologists, namely, that a section from the center of the bed of the ulcer out through the lip of the ulcer is the type of microscopic section and the extent of the microscopic section that is observed by pathologists in the *vast majority* of cases that come through the laboratory as the routine microscopic examination. I am well aware that in controversial cases a more elaborate procedure of examining serial sections from sections made radially from the center of the crater in all directions is the procedure that would be used. But, on the other hand, only one of *these 8* cases was primarily considered by the pathologists as anything other than a routine examination when the case was finally closed by him in his formal report to the hospital, this one exception being sections Nos. 4 and 5 now under consideration.

This statement concerning a single section from the gross specimen is evidenced by the observation of gross specimens in various pathological laboratories of which I had made a tour with intent to view the gross pathological specimens for two purposes: First, to determine the surgical mortality as the result of the removal of the specimen and second, to determine the extent of microscopic examination on which the pathological report is based.

My second excuse for presenting this second half of the section to the pathologists is the most important, namely, it serves as a connecting link in the pathological proof that ulcers which are said by some to become malignant have 25 points of differentiation from those that do not have a malignant tendency. With this latter point in view an analysis of the reports of these 23 pathologists concerning this second half becomes of paramount importance because as it is seen in the following tabulation only three of the 23 pathologists considered this second half of this ulcer anything other than that of a simple garden variety ulcer (see Fig. 8 A, B, C, D).

NON-MALIGNANT	
Mallory, ulcer	Robinson, ulcer
Parker, ulcer	Stewart, ulcer
Lacassagne, ulcer	Bell, ulcer
Simard, ulcer	McWhorter, ulcer
Aschner, ulcer	Bertrand, type not stated
Klemperer, ulcer	Pritchard, marginal mucosa hypertrophy
Pappenheimer, ulcer	Ewing, not true cancer obviously
Gray, ulcer	
Geschickter, ulcer	MALIGNANT
Stout, ulcer	
Foot, ulcer	Jorstad, adenocarcinoma
Konzelmann, ulcer	Masson, ulcer with atypical cells
Martland, ulcer	Ewing, changes toward cancer
Rhea, ulcer	

NON-MALIGNANT

MALLORY. *Non-malignant*—ulcer. *Criteria*—Not given.

PARKER. *Non-malignant*—ulcer. *Criteria*—Not given.

LACASSAGNE. *Non-malignant*—ulcer. *Criteria*—No malignant tissue.

SIMARD. *Non-malignant*—ulcer. *Criteria*—Fixation and staining cannot permit study of one edge of the ulcer.

ASCHNER. *Non-malignant*—ulcer. *Criteria*—Not stated.

KLEMPERER. *Non-malignant*—ulcer in a hyperplastic gastritis. *Criteria*—Not stated.

PAPPENHEIMER. *Non-malignant*—gastric ulcer. *Criteria*—Not stated.

GRAY. *Non-malignant*—gastric ulcer with quite denuded area lined by fibrotic material. *Criteria*—In the margin of the ulcer there is the usual hyperplasia of the glands and inflammatory cellular infiltration. There are some hyperchromatic detached regenerative or degenerative epithelial cells but no more than might be expected in a chronic inflammatory reaction of this sort.

GESCHICKTER. *Non-malignant*—ulcer, penetrating. *Criteria*—Not stated.

STOUT. *Non-malignant*—penetrating ulcer. *Criteria*—(A) Considerable inflammatory reaction in the base and in the surrounding mucosa; (B) remarkable hemorrhages in adjacent mucosa and submucosa with phagocytosis of blood pigment.

FOOT. *Non-malignant*—subacute ulcer (acutely inflamed chronic ulcer). *Criteria*—No neoplastic cells found; any metaplasia at rim of ulcer may be explained on basis of response to irritation.

KONZELMANN. *Non-malignant*—chronic ulcer. *Criteria*—Nothing suggestive of neoplasm. Regeneration and degeneration (inflammatory) epithelial cell changes.

MARTLAND. *Non-malignant*—chronic ulcer. *Criteria*—Not stated.

RHEA. *Non-malignant*—chronic ulcer, marginal mucosa hypertrophy. *Criteria*—Not given.

ROBINSON. *Non-malignant*—chronic ulcer, chronic gastritis. *Criteria*—This slide is that of a chronic ulcer which shows at one margin some epithelial cells that jumbled a bit. This I believe is reparative process and not evidence of malignancy.

STEWART. *Non-malignant*—chronic gastric ulcer surrounded by areas of hypertrophic gastritis-glands slightly atypical. *Criteria*—Not stated except as type. "I'd like to call this ulcerating cancer but don't find any indication that it is." Simple chronic ulcer.

BELL. *Non-malignant*—benign chronic ulcer. *Criteria*—Lymphatic infiltration of floor in part. There is a layer of old granulation tissue over part of the floor.

MCWHORTER. *Non-malignant*—probably simple ulcer from what can be seen of the section. *Criteria*—Not stated.

BERTRAND. *Non-malignant*—type not stated. *Criteria*—No evidence of malignancy.

PRITCHARD. *Non-malignant*—there is a marginal mucosa hypertrophy but no carcinoma. *Criteria*—Not given.

EWING. *Non-malignant*—refused to state "yes" or "no" concerning malignancy. Type of lesion not true cancer obviously. *Criteria*—Cells atypical. Very marked hypertrophic gastritis. Atypical change of cells on the lip of the mucosa; not necessarily malignant. Peculiar in some respects especially in the overgrowth of the glands. His closing remark was—"He did not die of cancer, did he?" Later, he said, "It has a peculiar appearance, some characteristics of cancer; has changes that are atypical, changes toward cancer which are responsible for considering it not ordinary simple ulcer."

It was considered malignant by Jorstad and Masson; and considered changing toward cancer by Ewing. The names of these men are recorded in the order of their assurance of its being malignant.

MALIGNANT

JORSTAD. *Malignant*—there is a Grade 1—Adenocarcinoma. *Criteria*—There is a marked piling up of the glandular epithelium at the edge of the denuded area. There is a marked increase in the tubular strata at this point, almost a polypous formation, but at the base of this polypous area there is a definite invasion of the muscularis by glands or tubules, which show cells with hyperchromatic nuclei and an occasional mitosis. This is a Grade 1—Adenocarcinoma. The base of the ulcer has no epithelial lining. The layer shows the muscularis is mainly scar tissue, which is very vascular. There is very little round cell infiltration and this is limited to the upper strata, and there is a definite absence of round cell infiltration about the numerous small endothelial line spaces throughout. I find no evidence of malignancy in the base of the ulcer.

MASSON. *Malignant*—"Yes" type; simple ulcer with group of atypical cells in proliferation in the mucosa near the ulcer. In the submucosa a vessel, probably lymphatic, containing a voluminous and typical cell. *Criteria*—Further criteria not given.

EWING. *Malignant*—refused to state "yes" or "no" concerning malignancy. Type of lesion not true cancer obviously. *Criteria*—Cells atypical. Very marked hypertrophic gastritis. Atypical change of cells on the lip of the mucosa; not necessarily malignant. Peculiar in some respects especially in the overgrowth of the glands. His closing remark was "He did not die of cancer, did he?" Later, he said, "It has a peculiar appearance; some characteristics of cancer; has changes that are atypical—changes toward cancer which are responsible for considering it not ordinary simple ulcer."

Jorstad is placed first of those who considered this second half of this section as malignant, because of the fact that he definitely stated that it was malignant; furthermore calling it "Adenocarcinoma—Grade 1." He elaborately recorded the criteria on which this opinion was based.

Masson was placed second on the list because of the fact that he stated unequivocally that the lesion was malignant. However, in stating the type of lesion he did not use the word carcinoma or cancer. It must be understood, however, that we were conversing through an interpreter. In his written report on the criteria I think he believed it to be carcinoma, although he did not specifically say so. He refers to it as a simple ulcer with groups of atypical cells which are described under type of lesion and in the second clause "in the submucosa a vessel (or channel) probably lymphatic contains a voluminous amount of atypical cells." My analysis of this statement would lead me to believe that he considered this a simple ulcer on which the additional criteria described led him to believe there was a malignant degeneration.

Ewing was unwilling to say "Yes" or "No" and then made the following statement, namely: that there is no definite, clear cut, well defined line between a lesion which is malignant and one which is not malignant. He intimated the term "Precarcinomatous" might be applied to these borderline cases. He was incensed, perhaps justly so, that I had asked him to study intently this second half of this section which he had seen. I believe, however, incensed as he might have been by what he considered "trickery" that these carefully recorded remarks concerning this section, particularly his statement—"There is no well defined clear cut line between malignant and non-malignant lesions" and his chain of thoughts, as evidenced by his disconnected statement, will eventually cause this to be one of the most important pathological reports that he ever made.

All except three pathologists considered this a non-malignant ulcer yet they nearly all agreed that the other half of this ulcer was malignant. There was a tumor mass having unusual microscopic criteria with characteristic carcinomatous cells on one side and not on the other. Was the tissue adjacent to the carcinomatous cells part of the carcinomatous growth, new growth tissue, or was it inflammatory similar to that seen in the bed of sim-

ple benign ulcer? *That is the vital question* that makes this section well worth studying.

CASE VI. Mr. A. W. is perhaps the most important of this group; at least from my roentgenological and pathological observation.

On September 8, 1923, we made a negative diagnosis of lesion of the stomach and a positive diagnosis of postpyloric ulcer and cicatricial contraction of the cap. There was, however, no definite crater present. There was no pyloric stenosis and the stomach evacuated itself in normal time.

On December 23, 1930, seven years later, the report on the case shows the following findings, excerpts of which are here quoted (see Fig. 9A):—"In the lower part of the corpus of the stomach there is a small ulcer and immediately above this is a second area of induration. Below the ulcer there is considerable inconstant deformity of the antrum and pyloric canal. The cap is quite normal in appearance. *Diagnosis:* From a study of these roentgenograms I believe one is justified in making a positive diagnosis of organic lesion involving the pyloric end of the stomach and lesser curvature at the lower end of the corpus of the stomach. I believe that the varying gross deformities of the distal end of the stomach are due to scar tissue from previous or practically healed ulcer. Just above this on the lesser curvature is a small ulcer the excavation of which apparently extends down into the mucosa. Adjacent to this is a second area of induration which may be broad mucosa erosion or the beginning or end stage of a deeper ulcer. The findings as observed in these series of roentgenograms are not at all indicative of new growth. At the present time there is no evidence of previous deformity of the cap. There is slight functional gastric retention. There are no duodenal diverticula and the passage of the barium meal through the small intestine is normal. The appendix is patent and filled readily with barium."

A review of these films with the knowledge we have since acquired, would lead us now to consider this case as definitely one of the roentgenological jokers and the majority of roentgenologists who saw this series of films are of the opinion that the lesion is malignant, as based on the roentgenological findings, in spite of the fact that I did not so regard it at the time of our second examination.

The patient was operated on and died within a few days. The lesion (as shown in Fig. 9C) was considered non-malignant by all the men except Masson and he made a positive diagnosis of malignancy and gave his criteria on which he based his diagnosis. So far as I could get the criteria on which the other pathologists based their negative diagnoses of carcinoma on this case they have been recorded. Ewing stopped as he was studying this section, wiped off the slide and his lenses and remarked that there were some slightly atypical glands which might be regarded as precarcinomatous. He was the only one who in any way supported Masson in his positive diagnosis of malignancy. I believe that this section will probably go down in history as one of great significance, certainly of greater significance than any section it has been my privilege to study. And this section will be the subject of another article which I hope to publish later under the title, "Microscopic Criteria of Growing Lesions," in which communication, I am prepared to state that in spite of twenty-three out of twenty-four opinions to the contrary this section has none of the characteristics of simple benign ulcer.

NON-MALIGNANT	
Lacassagne, ulcer	Pappenheimer, ulcer (chronic peptic)
Mallory, ulcer	Foot, ulcer
Parker, ulcer	Klemperer, multiple ulcers
Simard, ulcer	Stout, multiple ulcers
Aschner, ulcer	Robinson, multiple ulcers
Geschickter, ulcer (simple peptic)	Gray, ulcer (duodenal)
Jorstad, ulcer (benign)	McWhorter, ulcer
Konzelmann, ulcer	Bertrand, type not stated
Martland, ulcer	Ewing (?), multiple ulcers
Rhea, ulcer	
Pritchard, ulcer (chronic active)	MALIGNANT
Stewart, ulcer	Masson, linitis plastica
Bell, ulcer (benign)	Ewing (?), precancerous

NON-MALIGNANT

LACASSAGNE. *Non-malignant*—ulcer. Hyperplastic; edematous. *Criteria*—No malignant tumor.

MALLORY. *Non-malignant*—ulcer. *Criteria*—Not given.

PARKER. *Non-malignant*—ulcer. *Criteria*—Not given.

SIMARD. *Non-malignant*—ulcer. *Criteria*—The edges of the ulcer cannot be studied.

ASCHNER. *Non-malignant*—ulcer. *Criteria*—Not stated.

GESCHICKTER. *Non-malignant*—simple peptic ulcer. *Criteria*—Normal mucosa to area of ulceration. No invasion of surrounding tissue. Normal without irregularity of cells.

JORSTAD. *Non-malignant*—benign ulcer. *Criteria*—(A) Base of this ulcer is made up of chronic inflammatory tissue that is practically scar formation. There is moderate multiple abscess formation in the subserosa; (B) mucosa at the edges of the ulcer is slightly piled up, but the tubules have a distinct outline, the nuclei are not deeply stained, and there is a striking feature that at each edge just at the base of the epithelium is an area of inflammation which quite well accounts for the hyperplasia.

KONZELMANN. *Non-malignant*—chronic ulcer. *Criteria*—Nothing suggestive of a neoplastic infiltration. Suppuration of mucosa. Chronic ulcer. Part of wall cut on bias.

MARTLAND. *Non-malignant*—chronic ulcer. *Criteria*—Numerous eosinophiles.

RHEA. *Non-malignant*—chronic ulcer.

PRITCHARD. *Non-malignant*—chronic active ulcer. *Criteria*—No tumor.

STEWART. *Non-malignant*—chronic gastric ulcer surrounded by polypi growth of mucosa. *Criteria*—Not stated.

BELL. *Non-malignant*—benign chronic ulcer. *Criteria*—(A) Extends deeply into muscle; (B) subacute inflammation deep under center floor.

PAPPENHEIMER: *Non-malignant*—chronic peptic ulcer. *Criteria*—Ulcer shows no unusual features except rather marked eosinophilic reaction.

FOOT. *Non-malignant*—chronic ulcer. *Criteria*—No neoplastic cells are present in the ulcer area.

NON-MALIGNANT—MULTIPLE ULCERS

KLEMPERER. *Non-malignant*—ulceration (multiple) evident. Possibly ulcerative gastritis. *Criteria*—Not stated.

STOUT. *Non-malignant*—not a neoplasm. Two ulcers. *Criteria*—Marked gastritis, marked inflammatory reaction in both.

ROBINSON. *Non-malignant*—two chronic ulcers, one showing evidences of healing. Chronic gastritis. *Criteria*—Not given.

GRAY. *Non-malignant*—chronic ulcer of the duodenum. *Criteria*—(A) There is usual glandular hyperplasia, hypertrophy, and infiltration of leucocytes and fibroblastic proliferation; (B) at some distance from ulcer, hypertrophic glands apparently.

MCWHORTER. *Non-malignant*—ulcer. *Criteria*—Chronic inflammation.

BERTRAND. *Non-malignant*—type not stated. *Criteria*—No evidence of malignancy.

EWING (?). *Non-malignant*—chronic hypertrophic gastritis, almost adenoma but not malignant; multiple peptic ulcers. *Criteria*—Some glands slightly atypical and might be regarded as precancerous.

MALIGNANT

MASSON. *Malignant*—linitis plastica. *Criteria*—Atypical diffuse infiltration of mucous cells at bottom of ulcer; mitosis.

EWING (?). *Malignant*—chronic hypertrophic gastritis, almost adenoma but not malignant, multiple peptic ulcers. *Criteria*—Some glands slightly atypical and might be regarded as precancerous.

Measured by the pathological yardstick the clinical, roentgenological, and surgical diagnoses were all correct. Why then should this case be of interest? Because in the next article I am going to present pathological criteria that will indicate that we were all wrong except Masson and Ewing.

CASE VII. (See Fig. 10.) There was a large ulcer on the lesser curvature (Fig. 10A) which did not heal as rapidly as one expected. The crater itself and the adjacent lip of the ulcer had no unusual characteristics, but in the entire gastric wall throughout the corpus and antrum there was much thickening, and this thickening was caused by a proliferation or growth of tissue in the submucosa. This thickening caused someone to liken it to pellagra because of its similarity to the thickening and edema as observed in the subcutaneous tissue of this disease. Not being interested especially in the crater itself, a section of the gastric wall (Fig. 10B) some distance from the crater was submitted to these various pathologists, not all of whom saw the section and those who did gave it less consideration than any of the other sections. We are, however, recording their findings as follows:

NON-MALIGNANT

Stout, no ulcer, not malignant gastritis
Foot, chronic polypi
Jorstad, hyperplastic inflammatory lesion
Pritchard, chronic follicular gastritis
Masson, interstitial gastritis
Simard, benign interstitial
Robinson, subacute gastritis
Pappenheimer, type not given
Mallory, chronic gastritis
Parker, chronic gastritis
Rhea, follicular gastritis
Geschickter, simple hypertrophy
Martland, benign
McWhorter, inflammatory
Gray, not stated

MALIGNANT

Bell, adenocarcinoma
Konzelmann, linitis plastica
Klemperer, never saw such a section

NON-MALIGNANT

STOUT. *Non-malignant*—no ulcer. Chiefly submucosal, fibrosis and edema which involves the muscular coats to a large extent. *Criteria*—(A) Inflammatory reaction in mucosa and muscularis chiefly; (B) cell types; plasma cell predominating; polymorphonuclear leucocytes and lymphocytes; (C) I am not acquainted with the stomach changes of pellagra. Linitis plastica is not a disease *per se*.

FOOT. *Non-malignant*—chronic polypi or hyperplastic gastritis. Suggests allergic reaction of some sort. *Criteria*—(A) No neoplastic cells found; (B) chronic inflammation of mucosa and wall with extraordinary numbers of eosinophil, leucocytes. Asthma? Animal parasites?

JORSTAD. *Non-malignant*—hyperplastic inflammatory lesion, not specific. *Criteria*—(A) Stroma infiltration of mucosa and edema of submucosa; (B) hyperplasia of mucosa glands; (C) not like linitis plastica as it is known to me; (D) pellagra, I could not express an opinion about.

PRITCHARD. *Non-malignant*—no tumor present. Chronic follicular gastritis. *Criteria*—Hyperplasia of follicles. Hyperplasia of cells of tunica propria, abundant plasma cells. Hypertrophy of muscularis mucosa? Edema of submucosa and muscularis. Infiltration of these coats with chronic inflammatory cells.

MASSON. *Non-malignant*—interstitial gastritis. *Criteria*—Edema of submucosa and muscles and sclerosis. Large swollen connective cells in the submucosa like a radiodermitis.

SIMARD. *Non-malignant*—benign interstitial gastritis and hypertrophic sclerosis. *Criteria*—Infiltration inflammatory of the mucosa and many lymph follicles. Sclerosis of submucosa and lymphoid infiltration of muscular layers.

ROBINSON. *Non-malignant*—subacute gastritis. *Criteria*—This section is interesting as there is an inflammation involving the whole thickness of the wall. Eosinophiles and plasma cells can be seen scattered through the muscle coat and serosa. There is marked edema of the mucosa and submucosa in addition to the cellular infiltration.

PAPPENHEIMER. *Non-malignant*—type not given. *Criteria*—This section shows a chronic submucous edema and fibrosis with hyperplastic lymph follicles. There is no suggestion of malignant growth in the section.

MALLORY. *Non-malignant*—chronic gastritis. *Criteria*—Not given.

PARKER. *Non-malignant*—chronic gastritis. *Criteria*—Not given.

RHEA. *Non-malignant*—no tumor. Follicular gastritis. *Criteria*—Chronic inflammation of mucosa, submucosa and hyperplasia of follicles.

GESCHICKTER. *Non-malignant*—simple hypertrophy. *Criteria*—Not given.

MARTLAND. *Non-malignant*—benign. *Criteria*—Not given.

MCWHORTER. *Non-malignant*—inflammatory. *Criteria*—See no evidence of neoplastic infiltration beyond the mucosa.

GRAY. *Non-malignant*—not stated. *Criteria*—(A) There is only slight superficial erosion or ulceration of the mucosa and a diffuse lymphocytosis and plasma cell infiltration of the stroma and wall; (B) the glands are hyperplastic.

MALIGNANT

BELL. *Malignant*—adenocarcinoma. *Criteria*—Not stated.

KONZELMANN. *Malignant*—linitis plastica. *Criteria*—Chronic gastritis with marked fibrosis of submucosa.

KLEMPERER (?). *Malignant*—states he never saw such a section.

CASE VIII. This last case is probably the most controversial of all from every aspect: clinical, surgical, pathological, and follow-up. The patient, a man in the fifties, presented himself for examination and the following is a copy of our report based on serial roentgenography, a roentgenogram of which is reproduced in Figure 11A. This case was so controversial that I am publishing the findings and diagnosis of our first report in full—verbatim.

On December 8, 1925, the roentgen findings were: On the posterior wall of the stomach near the lesser curvature about 2 inches proximal to the pyloric sphincter there is apparently a crater which is about the diameter of a 25 cent piece. In the oblique position there is evidence of induration on both sides of this crater.

Diagnosis: From a study of these roentgenograms I believe that one is justified in making a positive diagnosis of an ulcer on the posterior wall of the stomach near the lesser curvature, about 2 inches proximal to the pyloric sphincter. This ulcer is of the size in which it is almost impossible sometimes to differentiate

between a simple ulcer and an ulcerating new growth. About sixty per cent of these cases are new growth and the findings in the two hour examination somewhat indicate the fact that this is an ulcer in a new growth. I believe that we should re-examine this case in about 2 weeks to determine if possible the exact character of this lesion.

The attending surgeon, Dr. Andrews, who referred the case to me was taken seriously ill before the patient returned to him after having the x-ray examination and he did not leave his work in charge of anyone. Thus the patient did not receive this report or learn of its contents.

More than a year later, on February 8, 1926, the patient returned directly to me and inquired concerning what we had found the year previous. I was surprised and shocked to know he had not received our original report and immediately made another examination and the following is a report of our findings:

Roentgen findings: A serial examination made of the gastro-intestinal tract immediately after the ingestion of a barium meal shows the size, shape, and position of the stomach and the passage of the barium through the tract.

Stomach is hypertonic. Peristalsis: three cycle type; equal on greater and lesser curvatures except at the extreme pyloric end of the lesser curvature. Systole and diastole: Shown fairly distinctly. Pars pylorica: Fails to expand and contract in a normal manner, particularly on the lesser curvature, close to the sphincter. Cap: Somewhat deformed, rather larger than normal. Duodenum, Jejunum and Ileum: Shown distinctly. At the two-hour period the stomach is about half empty and the head of the column is in the terminal ileum.

Diagnosis: From a study of these roentgenograms I believe that one is justified in making a positive diagnosis of a pathological lesion involving the extreme pyloric end of the lesser curvature of the stomach. In this region I believe the mucosa and the muscular coats are attached to each other in such a way as to interfere with the gastric peristalsis and that the mucosa raises up into a fold just proximal to this area. I believe that the pouch which I interpreted as a crater in the previous films is due to this fixation between the muscular and mucosal coats.

There is a bare possibility that this area may be malignant but I do not believe there is sufficient roentgenological evidence to justify one in making a diagnosis at the present time.

Dr. Eugene Pool was consulted and when he saw the second series of films and read these two reports, he said, "Cole, can you say with certainty that this lesion is not malignant?" My answer was in the negative. His next remark was, "Then we will have to *look in* and see. I thought you maintained that by an x-ray examination you could determine whether a lesion was or was not malignant." Shortly after this the patient was operated on by Dr. Pool and as I entered the operating-room he introduced me to the visiting doctors as *having been* a great roentgenologist but that I must be getting senile because I used to be willing to make a positive diagnosis of cancer, whereas, in this case, I was unwilling to do so. At this stage of the operation he was able to observe and palpate a relatively large mass involving the pyloric end of the stomach which he said was undoubtedly cancer, and wondered why there was any hesitancy on my part in considering it so. I still maintained that from a roentgenological standpoint it was not typical of gastric cancer. Sections were prepared and were to be ready for study the following Friday morning. I was there bright and early before the pathologist had studied them. He then examined them carefully knowing that there was a controversy and made a negative diagnosis of cancer saying that it was a "simple ulcer." Pool was asked to come down from the wards and go over the sections with us and he attempted to persuade the pathologist, but Dr. Denton could not be budged in his opinion that it was a simple ulcer. This was in the latter part of May and the following October when I again took up the study of the "Correlation of Pathology and Roentgenology" I went to the hospital to get the gross specimen for photography. I then found that Dr. Denton was no longer the pathologist at the institution and that the gross specimen could not be found; that a microscopic section could be found and the diagnosis, at least in the registry had been changed from "ulcer" to "sarcoma." I then found that the pathologist had taken two microscopic sections, of which he gave me one (Fig. 11B) which was the better of the two. This section has been submitted to all twenty-four pathologists.

Some time after this when Pool more or less facetiously joshed me about some other incident, I recalled this incident and he maintained that the records never had been changed as they appeared on the chart and that Ewing had seen the section and had called it "sarcoma." At our co-ordinating conference Foot resented the insinuation and finally after a diligent search, found the block from which microscopic sections had been cut and had additional sections cut which we subsequently had stained with various stains but the diagnosis of the twenty-four pathologists was based on the same microscopic section that I originally obtained from Dr. Denton.

NON-MALIGNANT	MALIGNANT
Lacassagne, ulcer	Ewing, carcinoma
Masson, ulcer	Foot, carcinoma
Jorstad, ulcer	Bertrand, carcinoma
Simard, ulcer	Stewart, carcinoma
Martland, ulcer	Gray, adenocarcinoma
Pappenheimer, ulcer	Rhea, ulcer; secondary malignancy
Robinson, ulcer	
Stout, not simple ulcer	Pritchard, cancer on ulcer
Konzelmann, chronic ulcer	Broders, sarcoma (lympho)
Klemperer, pseudo-leucemic or leucemia	Geschickter, sarcoma (lympho)
Aschner, ulceration lymphomatous lesion	Bell, sarcoma (lympho)
McWhorter, inflammatory, probably syphilis	Mallory, lymphoblastoma
	Parker, lymphoblastoma

NON-MALIGNANT

LACASSAGNE. *Non-malignant*—ulcer, simple. *Criteria*—Not given.

MASSON. *Non-malignant*—ulcer. *Criteria*—Inflammatory nodule in the thickened submucosa, between the muscles. A few atypical cells, but too poor fixation to say more.

JORSTAD. *Non-malignant*—ulcer. Benign. *Criteria*—(A) Margins of ulcer are clear cut; (B) moderate hyperplasia; (C) dense round cell infiltration throughout the base of the ulcer.

SIMARD. *Non-malignant*—ulcer. Benign. *Criteria*—Poorly fixed and stained. Poor section.

MARTLAND. *Non-malignant*—ulcer. Benign chronic. *Criteria*—Not given.

TABLE I.—DATA REGARDING SPECIMENS EXAMINED

Case No.	Date	Name	Questionable lesions	Diagnosis	Pathological material		Surgeon	Hospital
					Gross	Micro-scopic		
1	Early	U. K.		Gastric ulcer		*	Gerster	Mt. Sinai
2	Early	U. K.		Gastric ulcer		*	Gerster	Mt. Sinai
3	Early	U. K.		Gastric ulcer		*	Gerster	Mt. Sinai
4	Early	U. K.		Gastric ulcer		*	Gerster	Mt. Sinai
5	Early	U. K.		Gastric ulcer		*		Unknown
6	Early	U. K.		Gastric ulcer		*		Unknown
7	Early	465	?	?		*		Unknown
8	Early	455	?	?		*		Unknown
9	Early	U. K.		Cancer		*		Brooklyn
10	Early	Mrs. C.		Gastric ulcer	*		Erdmann	Unknown
11	Early	U. K.		Angioneurotic edema		*	Lowry	Unknown
12	Early	Mr. P.		Gastric ulcer		*		Unknown
13	Early	Mr. S.		Gastric ulcer	*		Berg	Mt. Sinai
14	3- 6-24	Mrs. W.	? Sect. II	?		*	Blank	French
15	3-10-26	Mr. S.	? Sect. VIII	?		*	Pool	New York
16		Mr. V.		Cancer		*	Hanan	Fifth Ave.
17	-27	6318		Gastric ulcer		*		New York
18	10- 7-27	Mr. P.		Cancer	*	*		French
19	10-12-27	Mrs. C.	?	?	*	*	Bancroft	Fifth Ave.
20	11-24-27	Mr. D.		Cancer	*	*		Fifth Ave.
21	12- 9-27	Mr. S.		Gastric ulcer	*	*		Fifth Ave.
22	-28	U. K.	?	?		*		Beekman St.
23	1- -28	Mrs. O.		Gastric ulcer			Erdmann	
24	2-29-28	Mrs. C.		Carcinoma colon		*		
25	3- -28	Mr. R.		Normal stomach	*	*		Fifth Ave.
26	4-12-28	Mrs. D.	? Sect. VII	?	*	*	Roberts	Fifth Ave.
27	6- 5-28	Mr. R.		Gastric ulcer	*	*		Fifth Ave.
28	9-27-28	Mr. B.		Gastric ulcer	*			
29	10- -28	Mrs. G.			*		Ramsdall	
30	10- -28	Mr. G.		Cancer	*	*	Bancroft	Fifth Ave.
31	-29	H030-1050	?	?		*		Lenox Hill
32	1-10-29	Mrs. C.		Gastric ulcer		*	Perkel	Post Graduate
33	2- -29	Mr. C.		Gastric ulcer		*	Jacques	Mt. Sinai
34	3-11-29	Mr. B.		Gastric ulcer	*			Beekman St.
35	3-15-29	Mr. R.					Honan	Jersey City
36	9- -29	Mr. ?		Cancer	*			French
37	7-22-29	Mr. W.		Cancer	*		Roberts	Fifth Ave.
38	9- 2-29	Mrs. W.		Cancer	*			
39	3-25-29	Mrs. W.		Cap ulcer	*	*	Bancroft	Fifth Ave.
40	11- 8-29	Mr. C.		Anatomical specimen	*	*		French
41	12-17-29	Mrs. R.		Carcinoma colon	*			
42	1- -30	Mrs. B.		Gastric ulcer	*	*	Pool	New York

TABLE I.—DATA REGARDING SPECIMENS EXAMINED—Continued

Case No.	Date	Name	Questionable lesions	Diagnosis	Pathological material		Surgeon	Hospital
					Gross	Micro-scopic		
43	1- 8-30	Mr. R.		Cap ulcer	*	*	Bancroft	Fifth Ave.
44	1- 9-30	Mr. G.		Ulcer		*		Univ. of Minn.
45	3-19-30	Mr. S.		Anatomical specimen	*	*		Fifth Ave.
46	4- 3-30	Mrs. R.	?	?	*	*	Hill	Fifth Ave.
47	4- 7-30	Mr. V.		Gastric ulcer	*	*		Fifth Ave.
48	5-21-30	Mr. F.		Gastritis	*	*	Ramsdall	White Plains
49	8-20-30	Mrs. C.		Cancer	*	*	Bancroft	Fifth Ave.
50	10- 4-30	Mr. C.	? Sects. IV-V	?	*	*	Bancroft	Fifth Ave.
51	11- -30	Mr. C.		Cancer	*	*		Y. G. H.
52	12- -30	Mr. W.	? Sect. VI	?	*	*	Russell	Harbor
53	12- 1-30	Mr. S.		Anatomical specimen	*	*		Fifth Ave.
54	-31	Mrs. R.		Cancer	*		Bancroft	Fifth Ave.
55	2- 4-31	Mrs. L.		Granuloma colon	*		Bancroft	Fifth Ave.
56	3-17-31	Mr. C.		Cancer	*	*		Fifth Ave.
57	3-25-31	Mrs. L.		Ulcer cap		*	Stetton	Lenox Hill
58	4- 4-31	Mr. H.		Hypertrophic gastritis	*	*	Bishop	Fifth Ave.
59	4-10-31	Mr. G.		Gastric ulcer				
60	4-20-31	Mr. W.		Cancer	*	*	Bancroft	Fifth Ave.
61	4-21-31	Mr. R.		Gastric ulcer		*	Lowry	Beekman St.
62	6-13-31	Mr. B.	? Sect. III	?	*	*	Roberts	Fifth Ave.
63	7- 9-31	Mrs. C.		Cancer colon	*	*		Fifth Ave.
64	8-12-31	Mr. M.		Cancer	*	*	Falk	French
65	12- -31	Mr. P.		Cancer	*	*	Jonesoff	French
66	-32	Mr. C.	?	?		*		Univ. of Minn.
67	-32	U. K.		Gastric ulcer		*		Univ. of Minn.
68	1- -32	Mrs. W.		Cancer colon	*	*	Kave	Doctors
69	1-23-32	Mr. L.		Cancer	*	*	Falk	French
70	1-26-32	Mr. G.		Cancer	*	*	Roberts	Fifth Ave.
71	2-25-32	Mr. T.		Gastritis		*	Herman	Asbury Park
72	2-26-32	Mr. LaV.		Cancer		*	Bancroft	Fifth Ave.
73	3- 3-32	Mr. M.		Gastric ulcer		*	Bancroft	Fifth Ave.
74	3-15-32	Mr. W.		Anatomical specimen		*	Bancroft	Fifth Ave.
75	6- 1-32	M.		Ulcer	*	*	Edgerton	St. Francis
76	9-23-32	Dr. S.	? Sect. I	?	*	*	Erdmann	
77	10- -32	F.		Ulcer	*	*	Lowry	Beekman St.
78	12-19-32	Dr. S.		Myoma	*	*	Berg	Mt. Sinai
79	2- 1-33	K.						
80	3- -33	Mr. S.		Cancer		*	Sweet	Peekskill
81	5- 8-33	Mr. C.				*	Edgerton	St. Francis
82	6- 7-33	U. K.				*		Akron City
83	6-26-33	Mr. H.		Ulcer		*	Edgerton	St. Francis
84	8-28-33	Mr. B.	?	?	*	*	Falk	French
85	11-26-34	F.			*	*		New Rochelle
86	6- 4-35	Mr. M.			*	*	Knip	French
87	11- 1-35	Mrs. J.		Colon carcinoma	*	*	Germain	Boston

TABLE II.—SUMMARY OF PATHOLOGICAL REPORTS BY 24 PATHOLOGISTS

Case No.	Malignant			Carcinoma	Type of lesion		Father Time
	No	Yes	?		Sarcoma	Equivocal or two	
I	5	16	0	16	0	0	Died in 14 months
II	1	22	1	9	9	5	Alive and well after 12 years—in spite of 22 out of 24 reports of malignancy
III	1	13	2	6	7	3	Alive and well after 6 years
IV V	1 20	19 2	0 1	21 1	0 2	2 1 (Changes toward cancer)	Alive after 4 years—then lost track of
VI	21	1	1	1	0	1 (Pre-cancerous)	Patient died but probably neoplastic after operation
VII	14	2	1	2	0	1	Patient died after operation. General infiltration of entire submucosa—two or three times as thick as normal
VIII	12	12	0	6	3L.S. 2L.B.	1	Alive after 7 years—no gastric symptoms but some cardiovascular changes

PAPPENHEIMER. *Non-malignant*—non-carcinomatous; ulcer—chronic. *Criteria*—There is possibility of syphilis; extreme fibrous thickening of submucosa and perivascular lymphoid infiltrations rather suggest it.

ROBINSON. *Non-malignant*—ulcer—chronic with hyperplastic lymph follicle. *Criteria*—Base of ulcer shows typical chronic inflammatory reaction. At the margin of the ulcer there is a mass of lymphoid tissue. Some of the lymphocytes are larger than normal but I believe this is due to the effect of the adjacent ulcer and not neoplastic in nature.

STOUT. *Non-malignant*—not simple ulcer. *Criteria*—(A) Because of enormous fibrosis of wall without excavation and without complete destruction of the muscularis; (B) peculiar lymphoid infiltration.

KONZELMANN. *Non-malignant*—chronic ulcer non-neoplastic type. *Criteria*—(A) Not well enough stained for study of nuclear details; (B) position and arrangement of cells not like that of neoplasm; (C) area in the upper right corner of section might attract attention. Cells here are not neoplastic cells but gastric epithelium undergoing disintegrating changes with infiltration of inflammatory cells.

MCWHORTER. *Non-malignant*—inflammatory, probably syphilis. *Criteria*—Not given.

KLEMPERER. *Non-malignant*—pseudo-leucemic or leucemia. *Criteria*—Definite diagnosis impossible.

ASCHNER. *Non-malignant*—ulceration of lymphomatous lesion. *Criteria*—Requested blood picture.

MALIGNANT

EWING. *Malignant*—carcinoma, small cell. *Criteria*—Diffuse growth of small atypical polyhedral cells.

FOOT. *Malignant*—carcinoma—diffuse, at the rim of ulcer, near hole in the section. *Criteria*—(A) Anaplastic hyperchromatin cells, with numerous mitotic figures lying loosely in an alveolar stroma; (B) might be interpreted as lymphosarcoma, but special stain would decide point; (C) it appears to be epithelial rather than lymphocytic.

BERTRAND. *Malignant*—carcinoma. *Criteria*—(A) Grouping of cells; (B) cells atypical; (C) modification of staining; (D) atypical nuclei.

STEWART. *Malignant*—very malignant; carcinoma; solid. *Criteria*—(A) In one area groups of small polyhedral cells, too diffuse to be reconcilable with reticulum cells of lymphoid tissue present; (B) in one or two I think I find mucus.

GRAY. *Malignant*—adenocarcinoma. *Criteria*—(A) Tendency toward gland formation in very anaplastic epithelial growth; (B) growth is small; does not invade outer wall, but is more advanced in abnormal cell characteristics and is potentially more malignant than Case IV; (C) growth is surrounded by extensive lymphoid infiltration.

RHEA. *Malignant*—ulcer; secondary malignancy at one margin. Section poor. *Criteria*—Active gastric ulcer chronic with, at one margin, a diffuse small cell type of carcinoma (questionable sarcoma). Chronic follicular gastritis.

PRITCHARD. *Malignant*—superimposed upon a chronic ulcer. Chronic active gastric ulcer. *Criteria*—At one margin is a diffuse small cell carcinoma based on cell type area of involvement. There is also a chronic follicular gastritis.

BRODERS. *Malignant*—sarcoma (lympho). *Criteria*—Associated with inflammatory lesion.

GESCHICKTER. *Malignant*—sarcoma (lympho or rectic cell). *Criteria*—(A) Uniform proliferation of cells with large nuclei; (B) definite mitotic figures; (C) typical small nuclear and large cytoplasm.

BELL. *Malignant*—lymphosarcoma or leucemia. *Criteria*—Not given.

MALLORY. *Malignant*—ulcer—at one end of section a lymphoblastoma. *Criteria*—Not given.

PARKER. *Malignant*—ulcer—at one end of section a lymphoblastoma. *Criteria*—Not given.

An analysis of the pathological findings in this case gives one food for thought. Of the twenty-four opinions twelve were for and twelve against malignancy. Of the twelve who considered it malignant, six believed it to be carcinoma and six sarcoma or some other neoplasm. Of the four who considered the lesion lymphoblastoma or lymphosarcoma, two classified it as malignant and two classified it as non-malignant.

If we now go back and apply these facts to the clinical aspect of this patient, who presented himself for an x-ray examination one year before and then had another just prior to the operation, these facts become of practical significance. The patient, having a clinical history that did not aid in the diagnosis and two equivocal x-ray diagnoses, one for and one against malignancy, found himself compelled to submit to an exploratory laparotomy in order really to determine the diagnosis. At the time of the exploratory operation the surgical findings indicated beyond any question of doubt that the lesion

TABLE III.—SUMMARY OF CLINICAL, ROENTGENOLOGICAL, SURGICAL, AND PRIMARY PATHOLOGICAL DIAGNOSES

Case	Clinical diagnosis	X-ray diagnosis	Surgical findings	Primary pathological diagnosis	Follow-up
Dr. S., I.	Gall bladder disease	Gastric carcinoma	Dr. Erdmann—pyloric induration	Duodenal ulcer—no cancer	Died in 14 months
M. W., II	Ulcer	Large ulcer—probably malignant.	Dr. Blank—large ulcer	Sarcoma	Alive and well after 12 years
G. B., III	Cancer	Tumor mass—probably cancer	Dr. Kingsley Roberts—spherical tumor	Atypical carcinoma	Alive and well after 6 years
Mr. C., IV	Ulcer	Carcinoma	Dr. Bancroft—peculiar soft tumor	Chronic ulcer	Alive last we knew after 4 years
Mr. C., V—same as IV	Ulcer	Carcinoma	Dr. Bancroft—peculiar soft tumor	Chronic ulcer	Alive last we knew after 4 years
A. W., VI	Ulcer	Multiple ulcers	Ulcer	Multiple ulcers	Died after operation
Mrs. D., VII	Ulcer	Unusual ulcer	Ulcer	Ulcer	Died after operation
P. S., VIII	Equivocal	Probably cancer—1925; probably not cancer—1926	Dr. Pool—cancer	Ulcer 3–15–26 Lymphosarcoma 3–29–26 (after Ewing had reported it such); later Ewing called it carcinoma	Alive and well and free of gastric symptoms after 7 years. (Heart and hypertension)

In Cases I and IV the x-ray diagnosis was shown to be wrong by the primary pathological report, but was shown to be right by the vast majority of pathological opinions or by Father Time.

In Cases II, III, VII, and VIII where the x-ray report was equivocal and where one might hope and expect to depend on the pathological report for aid in the final diagnosis the combined evidence as derived from the primary pathological report, the overwhelming concensus of opinion of all 24 pathologists or Father Time, still left the final diagnosis as equivocal as the day the x-ray diagnoses were made.

Case VI is most important of all. There was an unanimity of clinical, roentgenological, surgical and pathological opinion that this lesion was a simple ulcer. Yet this case is to be used for the foundation on which to build the unorthodox microscopic criteria of neoplasms which I hope will be accepted for publication in this Journal.

was cancer and I believe the term "carcinoma" was used. *The primary pathological yardstick* based on a paraffin prepared section indicated that the surgical diagnosis was wrong. This time the fight was between the surgeon and pathologist. The "x-ray man" sat on the sideline and cheered. This report did not substantiate or disprove the roentgen diagnosis because we had an equivocal one each way and with the pathologists throughout the country equally divided, both as to malignancy and the type of lesion, the main question which Pool brought up—whether or not I was becoming senile because of my unwillingness to make a positive or negative diagnosis of malignancy—still remains unsolved.

I asked Ewing to sponsor this communication, and in his characteristic "to the point" way, he said, "No, you can use my data but you have nothing to add to the diagnosis of cancer. You are simply diagnosing the pathologists."

It is not the intent of this article to diagnose the pathologists' ability. On the contrary, my desire is to find a firm foundation on which someone can build a microscopic diagnosis of cancer out of stones that are acceptable to the majority of them. The fact that I had nothing to add to the diagnosis is, so far as Ewing knew then, true; particularly as it concerns this article. But this article does pave the way for one which does have something to do with the microscopic diagnosis of gastric lesions. I hope there may be interest enough in this article so that the second may be published at an early date.

Eleven of the pathologists who had seen these sections met at my office in May, 1933, for the purpose of reviewing the sections and defending their diagnoses. They even brought their own microscopes and discussed the great variances in opinions. Nearly 3 years later, after I had made a more intensive study of these 8 sections, a group of representative internists and surgeons met on January 29, 1936, to discuss the significance of the great divergence of pathological opinion as it applied to the problems of gastric cancer and ulcer: such problems as the accuracy of diagnosis; prognosis; indications for further extensive surgery; indications for radiotherapy; and particularly the consideration of the accuracy of the pathological report in determining whether some particular lesion in which a brilliant surgical or radiation cure was

accomplished was or was not a cancer; whether it was a malignant neoplasm, and also to discuss whether all of these terms mean the same thing.

There are a variety of reasons for this incomprehensible difference of opinion. They are as follows:

REASONS FOR DIFFERENCE OF OPINION

1. Different pathologists observe different microscopic findings when examining the same sections.

2. Even when they observe the same findings, some believe that they indicate malignancy, others non-malignancy.

3. Some pathologists base their opinion on a general impression. It is "like some other lesion they have seen before." Others record and analyze their findings and can tell why they think it is malignant and why it is carcinoma rather than sarcoma.

4. Haste in examining the section. The lack of care in searching for the criteria; working late in the afternoon when one is tired leads to many of the errors in pathological diagnosis. This reason is heartily endorsed by Ewing.

5. Lack of unanimity in terminology leads to apparent differences of opinion which are diminished or eliminated by the use of some terminology which is understood by the different pathologists.

6. Lack of agreement as to the exact meaning of certain common terms such as "anaplasia," "hyperchronasia," "cytoplasia" and even the term "undifferentiated" leads to confusion. Pathologists may even accept the same definition but not apply it to specific findings in identical sections.

7. Routine microscopic sections are so small that they are inadequate for a negative diagnosis of cancer. They may be satisfactory for a positive diagnosis but not for a negative one. And I believe that this is a very important factor in differences of opinion, especially in cases in which the identical section is not seen by each pathologist.

8. Single stains are inadequate. A hematoxylin and eosin stain is excellent for cytology but eminently unsatisfactory for studying architectural changes in the lesion.

SUMMARY AND CONCLUSIONS

A. In about one-quarter of the cases of gastric lesions, there was a difference of opinion among representative pathologists as to whether the lesion was malignant, and a still greater diversity of opinion as to whether the lesion was a carcinoma, a sarcoma, or some other neoplasm.

B. Opinions vary even more when they are based on a study of microscopic sections that are cut and stained in a routine manner, especially when only a single stain is used.

C. Ewing believes that the difference of opinion occurs in about 20 per cent of the cases.

D. Routine microscopic sections as cut and stained in more than 90 per cent of the institutions are inadequate to rule out the presence of a gastric cancer or neoplasm; a positive diagnosis of cancer may be made on such sections but not a negative diagnosis.

E. The pathologists mentioned rate above the average and, if there is as much diversity of opinion among them as herein shown, there would be an even greater difference of opinion among those less experienced.

F. This difference of opinion as to the pathology present in gastric lesions astonishes the internist and the surgeon and some pathologists, but why should it?

G. A similar difference of opinion as to pathology in bone tumors has been known to exist since Codman started the bone sarcoma registry.

H. Ewing now maintains that the pathologist encounters the same difficulty in the diagnosis of gastric lesions that he is known to have encountered in the diagnosis of bone lesions.

THE EFFECT OF THIS DIFFERENCE OF OPINION ON SURGICAL STATISTICS

Statistics as to surgical cures in gastric cancer cases and statistics on simple gastric ulcers that have become malignant should not be based on a single pathological report. Moreover, in cases in which a long surgical cure of gastric cancer is reported, a critical review of the section should be made by a group of pathologists such as these: but even then, where does it get one in determining the ac-

curacy of statistics, especially if one bears in mind sections 2, 3, 6, and 8. Should Drs. Blank, Roberts, Bancroft, and Pool receive credit for surgical cures on these cases? I am not saying whether they should or should not, I am just asking the question. Is the pathological yardstick a sufficiently accurate instrument with which to measure the errors in clinical, roentgenological, and surgical diagnoses? May not the clinician, roentgenologist, or surgeon question the pathological diagnosis when it is definitely at variance with their findings?

Bearing in mind the findings herein reported, it is doubtful if pathology can be used as such a yardstick. In these 8 cases the pathologists found no clear cut line between those which are malignant and those which are not malignant. Ewing says there is no clear cut line between a lesion which is a cancer and one which is not a cancer. One finds all gradations of change in the mucosa from atropic gastritis through hypertrophic gastritis, precarcinomatous changes, undifferentiated cells, up to the differentiated group of cancer cells in which there is little or no question as to the pathological diagnosis. Ewing defends the term "precancerous" as one which is necessary to describe a certain condition but he says that cases showing *only* precancerous changes cannot be claimed as surgical cures.

NEW OBSERVATIONS AND CONSTRUCTIVE SUGGESTIONS

Ewing says that the real pathological problem is not whether a lesion is malignant or non-malignant but whether it is neoplastic or inflammatory. He refers to this as a problem, something that should be solved. Microscopic findings not observed or used as criteria by any of the pathologists in studying these eight sections give ample material with which to solve this problem of the differentiation of neoplastic and inflammatory lesions. This is particularly true when the findings are compared with the simple "garden variety" of gastric ulcers.

Case VI which was considered a simple ulcer by 22 of 23 pathologists is one which suddenly and violently attracted my attention to this subject in the last week of December, 1930, and even at that time I showed it to Ewing as an unusual case but it did not attract his attention. Of the 23 pathologists who saw this case Masson was the only one who believed it to be malignant and he considered it a linitis plastica. Later Ewing in reviewing this considered it possibly precancerous. Everyone else considered it a simple gastric ulcer.

After having intensely studied the microscopic findings of the common garden variety of gastric ulcer, the moment I saw this section it was evident to me that it was not a common garden variety and therefore even then we, my associates and myself, referred to it in our own conversation as the "hot-house variety" of ulcer in contradistinction to the "common garden variety" of ulcer with which we were familiar. When I first saw this section I was completely at sea as to drawing conclusions from the findings observed in it, and made the following entry in my diary concerning it.

"Friday, Jan. 23, 1931

Just received 48 excellent sections of the three ulcers of A. W. A brief look at these confirms my suspicion of the gross specimen, viz., that this is not the garden variety of ulcer. I fear these findings will completely disrupt the picture puzzle of gastric ulcers which, up to the present, has progressed so favorably. Each piece of the jig-saw interlocked accurately. I can't see how these findings will fit into the picture of the thrombotic pathogenesis or even of a lesion beginning with the outer coats and breaking through. Or, if the sections prove to be malignant, the lesion is of such an infinitesimal size that it does not correspond with my previous conception of fair size area of malignancy that has ulcerated in its center. My architect, Mr. Bevin, said that some famous architect had said that a problem should be converted into a feature. Applied to this problem I certainly am wondering about converting these sections of A. W. into a feature."

It was not until I observed another similar lesion from which four or five sections were cut that I began to comprehend the significance of the findings observed in section No. 6. These two sections, Nos. 4 and 5, from another lesion became the key that unlocked the problem of differentiation of neoplastic from inflammatory lesions and when the findings observed in these 2 cases are compared with those of 6 other sections, the problem of

the diversity of opinion in these 8 sections is greatly simplified.

Section No. 4 has more than 50 points that differentiate it from the findings observed in the simple common garden variety of ulcer; that is, there are 25 findings in this section that are the direct antithesis of 25 findings observed in the common garden variety of ulcer. I believe that I am correct when I state that not a single one of the 25 criteria was recorded in the reports of the criteria of any one of the 24 pathologists. Each one of these 25 criteria is of such great significance that a definite conclusion can be drawn from it. Whether such conclusions are rational or irrational, time only will tell. I am hoping that this presentation will attract sufficient interest so that these 25 points of differentiation of new-growing tissue (I shall avoid the term neoplastic) from inflammatory lesions may be accepted by this journal for early publication.

BIBLIOGRAPHY

1. BREWER, GEORGE, and COLE, L. G. The roentgenologic diagnosis of surgical lesions of the stomach and duodenum. Ann. Surg., 1915, 61: 55–72.
2. COLE, LEWIS GREGORY. J. Am. M. Ass., 1912, 59: 1947–1951; The positive and negative diagnosis of gastric cancer by means of serial roentgenography. New York M. J., 1914, Feb.
3. Idem. Gastric cancer: correlation of roentgenological and pathological findings. Am. J. Surg., 1936, 31: 206–224; 257–259.
4. COLE and COLLABORATORS. Radiologic Exploration of the Mucosa of the Gastro-Intestinal Tract. St. Paul and Minneapolis: The Bruce Publishing Co., 1934.

THE PREVENTION OF POSTOPERATIVE JEJUNAL ULCERS BY DIET AND FUNDUSECTOMY

An Experimental Study in Dogs

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In a previous study (11) the value of certain medical procedures for the prevention of jejunal ulcers in dogs operated upon by the Mann-Williamson technique was determined. During the course of these studies our attention was attracted to the report of Connell (1, 2, 3), who suggested fundusectomy as a method for decreasing gastric secretion. Having, previous to the report of Connell, performed subtotal gastrectomy (4) in a series of dogs in which at least two-thirds of the stomach was removed and in which gastric acidity returned to normal in from 3 to 5 months, we thought that fundusectomy might delay, but not prevent, the development of jejunal ulcer. However, we have found that the administration of a nutritious, easily digested diet plus fundusectomy has prevented jejunal ulcer from occurring in all of 13 dogs, 6 of which have survived more than 2 years after operation.

It should be pointed out that the experimental ulcer which occurs after the Mann-Williamson operation (gastrojejunostomy and drainage of bile and pancreatic juice into the last 15 centimeters of the ileum) is believed to be quite analogous etiologically to postoperative jejunal ulcer in man. In the course of our previous studies (11), it was found that the majority of these animals secrete a gastric juice of "normal" average acidity, but continue to secrete in response to a meal for a longer period of time than normal animals, which confirmed the report of McCann. Thus, we have in these animals a gastric juice of normal acidity coming into contact with the more susceptible (more susceptible to acid irritation than the duodenal, ref. 5) jejunal mucosa for a comparably longer period of time (due to retention, hypersecretion, or both) in addition to the fact that the neutralizing and diluting action of pancreatic juice and bile is absent. From our studies and those of others (7, 8, 9, 10), it would appear that acid irritation is the chief factor in the etiology of the ulcer. Yet, we believe that nutritional and mechanical factors, particularly the former, play an important adjunctive rôle in the rate of onset and of lethal hemorrhage or perforation. The results that follow show clearly the rôle that nutrition plays.

METHODS

In any therapeutic study an adequate control series is essential for a trustworthy interpretation of the results. In our previous therapeutic study (11) a series of 42 control animals served as a basis for the interpretation of the therapeutic results. This control series may also be used for this study. Referring to Figure 1, curve *A* represents the survival-time curve for the 42 control dogs. For example, all had died with ulcer at 17 weeks; 50 per cent at 11 weeks. Curve *B* represents the time of diagnosis of ulcer in 22 of the dogs, the diagnosis being made by observing the presence of "tarry stools" or gross blood in the gastric contents.

In performing the fundusectomy, a wedge-shaped portion of the fundus was removed by the incisions indicated in Figure 2. This resulted in the removal of at least two-thirds and frequently three-fourths of the acid-secreting mucosa, the variation in the amount removed being due to differences in facility of exposure of the stomach. The fundusectomy was performed 3 or 4 weeks prior to the Mann-Williamson operation.

Four groups of experiments were performed. Group I: In the first group fundusectomy was performed and then the Mann-Williamson (7) operation, after which the animals were placed on the stock diet (ground parboiled meat, bread, and milk) plus raw pancreas (200 grams daily). Group II: These animals in Group I being deprived, for the larger part, of

TABLE I.—APPROXIMATELY 75 PER CENT OF THE FUNDUS WAS REMOVED. THIS DOES NOT DISTURB NUTRITION. THEN A MANN-WILLIAMSON OPERATION WAS PERFORMED ONE MONTH LATER. THE "STOCK DIET" WAS FED.

Number of dogs operated upon..	11
Survival time after Mann-Williamson.....	6 to 15 weeks
Average survival time.....	10 weeks
Jejunal ulcers.....	3, per cent incidence 27
Prophylactic value in dogs not developing ulcer as calculated from Curve B, Fig. 1	63 per cent

Remarks.—In these dogs, the gastric remnant underwent hypertrophy. Gastric acidity gradually returned toward normal.

both gastric and pancreatic digestion lost weight rapidly. So, it became necessary to devise a diet that was more easily digested and absorbed. This was done; but since we had changed the diet it was necessary to determine the effect of the new diet on the occurrence of ulcer. This was done and constitutes the experiments in Group II. Group III: In the third group of experiments, fundusectomy was done, then the Mann-Williamson, after which the dogs were given the special diet. Group IV: Same as Group III, except gastric blood vessels were ligated instead of performing a fundusectomy.

RESULTS

Group I. Fundusectomy, Mann-Williamson operation, and a stock diet. The results obtained in the experiments, in which a fundusectomy was followed by the Mann-Williamson operation and the animals placed on a stock diet, are shown in Table I. In the 11 dogs so treated only 3 developed jejunal ulcer. The ulcers were found in the dogs that survived longest, or in which the acidity returned to about normal average values. The animals lost weight rapidly in spite of the relatively large amount of food they consumed. The results indicated to us that if we could control the nutritional factor the story might be different. This stimulated us to perform the following group of experiments which involved the feeding of a nutritious easily assimilated diet.

Group II. The effect of a special diet, more easily assimilated, on the occurrence of jejunal ulcer in Mann-Williamson dogs. After considerable preliminary experimentation with diets, the following diet was chosen as the one to be used in our experiments.

TABLE II.—EFFECT OF THE SPECIAL DIET ON THE OCCURRENCE OF JEJUNAL ULCER

Dog No.	Duration after operation survival time weeks	Presence of ulcer	Weight loss per cent	Remarks
Group 1				
1–13	9	None	33	Distemper, gastro-enteritis
2–26	9	None	20	Distemper—adhesions
3–25	9	None	33	Obstruction—intra-abdominal hernia
4– 8	10	Ulcer	45	Pneumonia—anemia—cachexia
5– 4	11	None	20	Pneumonia—cachexia
6–27	11	None	18	Epidermic encephalitis
7–15	14	Ulcer	30	Hemorrhage
8– 6	15	None	25	Obstruction—intra-abdominal hernia
9– 9	15	None	40	Cachexia—pneumonia
10– 2	16	Ulcer	32	Hemorrhage
Group 2				
11–18	20	Ulcer	10	Hemorrhage
12–21	25	Ulcer	Gained	Perforation—normal weight at death
13–22	41	Ulcer	Gained	Perforation: ulcer large and indurated
14–19*	20	Ulcer*	No change	Developed ulcer at 20 weeks—placed on mucin—ulcer healed. Distemper
15–16	82	None	Gained	Anesthetized at 82 weeks—no ulcer
16–14	26	Ulcer	19*	Hemorrhage—*lost weight after developing ulcer
17–12	31	Ulcer	33*	Hemorrhage and cachexia—*most of the weight loss occurred after hemorrhage started
18–10	30	Ulcer	No change	Perforation. Ulcer very large and indurated
19– 3*	30	Ulcer*	Gained	Developed ulcer at 30 weeks; placed on mucin-at 14 months-killed-ulcer healed
20– 1	58	Ulcer	Slowly lost weight last 3 mo.	Perforation—ulcer large and indurated

*Ulcer developed and healed on gastric mucin therapy.

SPECIAL DIET

High in nuclear substances, vitamins and readily assimilable carbohydrates.

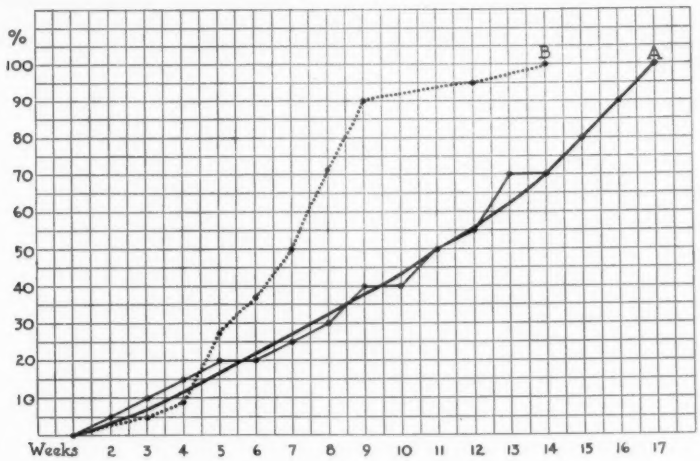

Fig. 1. Curve *A* shows the percentage-time survival of 42 Mann-Williamson dogs. Curve *B* shows the percentage-time of onset of ulcer in 22 of the dogs as determined by clinical diagnosis (gross blood in stools or gastric contents).

	Per cent	Grams
A prepared dog food		400
Wheat and barley flour	75	
Dried milk	10	
Tomatoes	5	
Bone meal	5	
Cod liver oil and NaCl	5	
Fresh whole milk		200
Raw ground pancreas		300
Raw ground liver		200
Corn syrup		100
Banana flour		50

This diet (2.6 pounds) constituted the minimum daily ration. When the dogs consumed this ration, which generally occurred, they were given an additional supply. Most dogs consumed 4 pounds of the food mixture daily, others 6 pounds. Obviously the fecal wastage was large.

The results are shown in Table II. First, it is to be noted that no deaths with ulcer occurred prior to 10 weeks. In the 10 dogs surviving less than 17 weeks, which was the maximal survival time of the control dogs (Fig. 1, Curve *A*), only 3 had an ulcer. In the 10 dogs surviving longer than 17 weeks, all but 1 developed an ulcer. The incidence of ulcer in the 20 dogs was 60 per cent; in the dogs surviving 20 or more weeks it was 90 per cent. Thus, the special diet delayed the development of an ulcer and the onset of lethal hemorrhage and perforation. In this regard the difference in the weight loss between the first and second groups of 10 animals each is especially striking.

Group III. Fundusectomy plus the special diet. In these experiments the fundusectomy was performed, then a month later the Mann-Williamson operation, after which the animal was placed on the special diet.

In none of the 13 animals so treated did ulcer occur; 7 survived longer than 1 year, and 6 more than 2 years without developing ulcer. The 6 surviving longer than 2 years were in excellent condition when chloroformed.

The average pre-operative gastric emptying time to the test meal was 3 hours and 30 minutes; 1 month after fundusectomy it was 3 hours and 15 minutes; and 6 months after the Mann-Williamson operation 3 hours and 50 minutes. The pre-operative average gastric emptying time for 6 dogs surviving for 2 years was 3 hours and 30 minutes; at 2 years after operation the average emptying time was 4 hours.

In the 6 dogs surviving for 2 years, the acid values of the gastric contents had returned to the normal range after 1 year, which has been observed by others. The same was true at 2

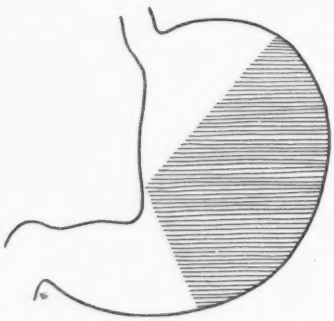

Fig. 2. Shaded area shows approximately the amount of fundus removed.

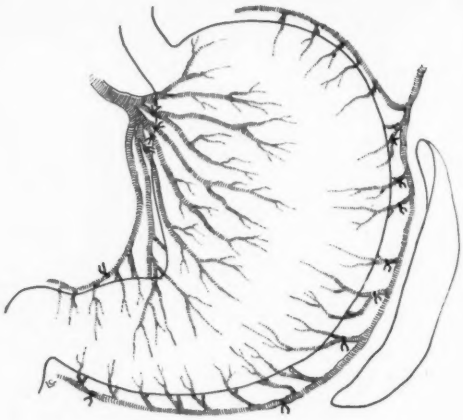

Fig. 3. Shows the vessels ligated.

years. However, the average free acidity of the 6 dogs at 4 hours was 20 per cent less than the control free acidity, which is insufficient in view of the variations in gastric acidity to warrant emphasis. Of greater significance, we believe, is the fact that the average volume of the gastric contents at 4 hours after meals was 68 cubic centimeters, while in 7 Mann-Williamson dogs, not fundusectomized but fed the same diet and test meal, the average 4 hour post-cibum volume was about 150 cubic centimeters. This marked dilution of the gastric contents at 4 hours is the most constant and striking finding resulting from gastric analysis in Mann-Williamson dogs that we have observed. In view of the acid values, this fact is not easy to interpret, and would merit interpretation only provided we had data on the neutral chlorides, which assay was not made. When the total gastric contents obtained by aspiration at 4, 6, and 8 hours in the 6 fundusectomized dogs is summed up and averaged, the results are 68, 40, and 6 cubic centimeters, which is in contrast to 146.3, 36.0, and 8.8 cubic centimeters for 6 non-fundusectomized (Mann-Williamson) dogs. This shows that the fundusectomized dogs either do not form as much gastric secretion as, or show less retention than, ordinary Mann-Williamson dogs; that is, gastric contents of about normal acidity is emptied for a shorter period of time into the jejunum of fundusectomized dogs than into the jejunum of non-fundusectomized Mann-Williamson dogs.

To examine these observations further, we determined the response of 5 2-year fundusectomized animals and of 5 non-fundusectomized Mann-Williamson dogs to histamine. This was done by emptying the stomach, then injecting 1 milligram of histamine (ergamine acid phosphate) subcutaneously and evacuating the stomach at 10 minute intervals for 1 hour. The results shown in Table IV indicate that the fundusectomized Mann-Williamson animals respond almost normally to histamine, but definitely less than the non-fundusectomized Mann-Williamson. This would appear to constitute very clear evidence of an increased volume of secretion in non-fundusectomized dogs as compared with fundusectomized. But the evidence is not as clear as it might be because the non-fundusectomized dogs have an ulcer and the fundusectomized do not, and when the histamine test was applied to non-fundusectomized Mann-Williamson animals during the first 3 to 5 weeks after operation, when no ulcer is present, we obtained only a slight increase in the volume of juice secreted in response to histamine over that secreted by normal dogs. Unfortunately, we could not settle the matter on a larger series, because the advisability of performing the histamine test did not occur to us until this work was practically completed. Thus, we do not know whether the increased response to histamine is due to the ulcer or not.

TABLE III.—EFFECT OF FUNDUSECTOMY PLUS THE SPECIAL DIET ON THE OCCURRENCE OF JEJUNAL ULCER

Dog No.	Duration after operation	Presence of ulcer	Weight loss per cent	Remarks
1	37 wks.	None	Gained	Pneumonia
2	8 wks.	None	No change	Obstruction
3	2 yrs. 3 mo.	None	Gained	Chloroformed—condition excellent
4	2 yrs. 1 mo.	None	Gained	Chloroformed—condition excellent
5	2 yrs. 2 mo.	None	Gained	Chloroformed—condition excellent
6	2 yrs. 1 mo.	None	Gained	Chloroformed—condition excellent
7	18 wks.	None	33	Cachexia
8	1 yr. 3 mo.	None	No change	Pneumonia
9	2 yr. 2 mo.	None	No change	Chloroformed
10	45 wks.	None	20	Not ascertainable
11	17 wks.	None	No change	Pneumonia
12	33 wks.	None	30	Gastro-enteritis (?)
13	2 yrs.	None	No change	Chloroformed at 2 yrs.

TABLE IV.—THE RESPONSE OF THE NORMAL, FUNDUSECTOMIZED (2 YR.) AND NON-FUNDUSECTOMIZED MANN-WILLIAMSON (4 MO.) DOG'S STOMACH TO HISTAMINE

Operation	Dog No.	Volume c.cm. 1 hr.	Acidity		Remarks
			Free per cent	Total per cent	
Normal	1	42.0	0.118	0.200	No ulcer
	2	64.0	0.218	0.264	
	3	72.0	0.127	0.191	
	4	45.0	0.218	0.346	
Average		53.	0.170	0.250	
Fundusectomized Mann-Williamson operation	1	38.0	0.118	0.136	No ulcer
	2	46.4	0.118	0.237	
	3	65.0	0.118	0.145	
	4	77.8	0.136	0.228	
	5	26.5	0.082	0.091	
Average		50.7	0.114	0.167	
Non-fundusectomized Mann-Williamson operation	1	215.0	0.273	0.300	Has ulcer
	2	126.0	0.228	0.320	Has ulcer
	3	135.0	0.200	0.410	Has ulcer
	4	107.0	0.109	0.319	Has ulcer
	5	77.0	0 173	0.309	Ulcer questionable
Average		132.0	0.216	0.350	

Another factor which has been borne in mind in interpreting the foregoing results is the factor of retention, which is beyond control in such studies. Yet, it is clear that the acid factor is operating over a longer period of time in the non-fundusectomized animals, if not in a greater quantity.

In this connection, attention should be called to the occasional occurrence of jejunal or marginal ulcer in a human patient with a rapid emptying stomach following gastrojejunostomy or subtotal resection. In most such patients gastric analysis shows either relatively little secretion of acid, or that it is difficult to obtain. From animal studies we know that distention of the intestine usually inhibits gastric secretion; but if the intestine has compensated for or adapted itself to the inhibitory distention factor, the intestinal phase of gastric secretion may become evident. In such an instance no food being present in the stomach, uncombined acid or "raw" gastric juice will pass into jejunum to irritate it and predispose to ulcer.

At autopsy 5 of the 6 animals (no ulcer present) manifested to a more or less extent the peculiar tubular form of the pyloric antrum shown in Figure 4. The interpretation of this finding is not clear. In addition, 4 of the 6 animals showed the presence of a chocolate brown pigmentation of the intestine involving the musculature, but not the mucosa. The colon was likewise pigmented in 4 of the 6. This was noted by Mann and Graham in their gastrectomized dogs; but we have never seen it in our gastrectomized animals. The histology of the phenomenon is being studied by Dr. L. B. Arey.

Group IV. The effect of ligating a portion of the blood supply of the stomach on the occurrence of jejunal ulcer. Since the secretion of any secretory organ is related to its blood supply, we decided to try the effect of ligating some of the major vessels which supply the fundus of the stomach instead of performing a fundusectomy. This procedure has the merit that it is a simple operation, but has the very definite disadvantage of being a less quantitative procedure.

In 11 animals the blood vessels shown in Figure 3 were ligated and a Mann-Williamson

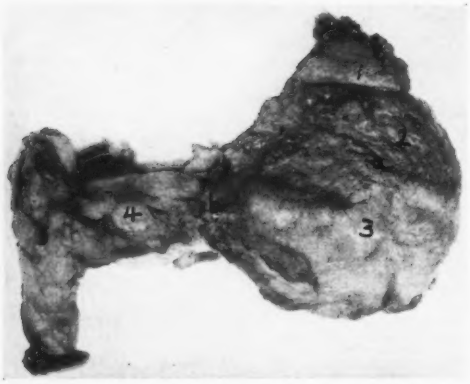

Fig. 4. This photograph shows the peculiar tubular form of the pyloric antrum observed in 5 of the 6 fundusectomized animals living more than 2 years. *1*, Diaphragm; *2*, the cardia; *a*, the suture line after fundusectomy; *3*, the hypertrophied segment; *b*, junction of hypertrophied segment with the tubular pyloric antrum; *4*, the pyloric antrum; *5*, the jejunum, with end-to-side anastomosis of pyloric antrum to it. This specimen was selected also to demonstrate the stomach that showed the most adhesions, it being noted that the hypertrophied portion is free from adhesions.

operation performed, the special diet described being fed. The results are shown in Table V. The development of the ulcer was definitely delayed in one (dog 7) and prevented from developing for 18 months in 3 (dogs 1, 2, and 4). In the 3 latter animals the stomach on being analyzed by a test meal and histamine, reacted at 18 months just as if two-thirds or three-fourths of the fundus had been removed. It is obvious from the results, however, that the procedure is not as uniformly effective as fundusectomy, as might have been predicted.

TABLE V.—EFFECT OF LIGATING GASTRIC BLOOD VESSELS PLUS THE SPECIAL DIET ON THE OCCURRENCE OF JEJUNAL ULCER

Dog No.	Duration after operation	Presence of ulcer	Weight loss per cent	Remarks
1	18 months	None	Gained 6 lbs.	At 18 months reacts to histamine as a normal animal. Chloroformed—no ulcer
2	18 months	None	Gained 7 lbs.	At 18 months reacts to histamine as a normal animal. Chloroformed—no ulcer
3	17 weeks	Ulcer	None	Perforated ulcer, peritonitis
4	18 months	None	Gained 6 lbs.	Chloroformed—no ulcer
5	15 weeks	None	Gained	Mysenteric thrombosis
6	8 weeks	Ulcer	40 per cent	Perforated ulcer
7	52 weeks	Ulcer	12 per cent	Perforated ulcer
8	12 weeks	Ulcer	40 per cent	Perforated ulcer
9	11 weeks	Ulcer	30 per cent	Perforated ulcer
10	13 weeks	Ulcer	40 per cent	Perforated ulcer
11	13 weeks	Ulcer	25 per cent	Perforated ulcer

DISCUSSION

The literature on the effect of subtotal fundusectomy has been reviewed by Seely and Tollinger. The results are practically unanimous in showing that after 6 to 8 months the free and total acidity returns to almost normal average values. This is to be anticipated in view of the remarkable property of the stomach to undergo dilation and hypertrophy, so that as long as any acid forming cells are left in place it is simply a matter of time until normal acid values are observed. Yet, the mere titration of the acidity of the gastric contents does not necessarily yield a correct picture of the acid that is available for irritating the jejunum, because the volume of acid secreted, and the duration of time over which it is secreted or is passed into the jejunum must obviously be considered. It is in these latter respects that our 2-year fundusectomized dogs with a Mann-Williamson operation differed from the non-fundusectomized. It is chiefly this reduction in quantity and particularly in the duration of contact of secretion with the jejunum, plus the easily assimilable diet which explains the failure of our fundusectomized animals to develop ulcer even after 2 years. Indeed, it appears that no other reasonable explanation is possible.

Of course, it is possible that our animals may have developed ulcer at 2½ or 3 years. If their gastric response should have returned to that of non-fundusectomized animals, or if they should have started to lose weight, they would certainly, in our experience, based on about 170 such animals, develop ulcer. As we have pointed out elsewhere, totally gastrectomized dogs, pigs, rats, or monkeys (we have now had experience with at least 70 gastrectomized animals living for 1 to 10 years) do not develop duodenal or jejunal ulcer, although some may suffer "ups and downs" in

their nutrition and digestive condition. However, we shall intentionally avoid commenting or expressing an opinion on the promise of fundusectomy as a surgical procedure for the control of peptic ulcer in man. The results of well controlled animal experiments provide evidence which serves to direct clinical efforts and upon which to base the interpretation of clinical results.

SUMMARY

1. Fundusectomy has some prophylactic value in the prevention of jejunal ulcer in dogs operated upon by the Mann-Williamson technique and fed an ordinary diet.

2. It was found that the feeding of an easily assimilable diet to non-fundusectomized Mann-Williamson animals delayed the onset of jejunal ulcer and of lethal perforation and hemorrhage.

3. The combination of the special diet and fundusectomy prevented the development of jejunal ulcer in all of 13 animals, 6 of which survived 2 years or longer. Gastric analyses revealed a gastric acidity of normal values in the animals surviving for more than 2 years, but the acid "available" for more prolonged irritation of the jejunum was definitely less in the fundusectomized than in the non-fundusectomized animals.

4. These experimental therapeutic results emphasize the importance of the nutritional (disturbance of digestion) and particularly the acid factors in the causation of postoperative jejunal ulcer.

REFERENCES

1. CONNELL, F. G. Fundusectomy; experimental. Surg., Gynec. & Obst., 1931, 53: 750.
2. Idem. Resection of fundus of stomach from peptic ulcer. Ann. Surg., 1932, 96: 200.
3. Idem. Partial gastric fundusectomy in treatment of peptic ulcer. Surg., Gynec. & Obst., 1934, 59: 786.
4. FAULEY, G. B., STRAUSS, H. A., and IVY, A. C. Studies on effects of subtotal gastrectomy in dogs. Am. J. Surg., 1932, 17: 427.
5. IVY, A. C., and FAULEY, G. B. A study of the chronicity factors in peptic ulcer. Am. J Surg., 1931, 11: 531.
6. MANN, F. C., and GRAHAM, A. S. Gastrectomy, an experimental study. Ann. Surg., 1932, 95: 455.
7. MANN, F. C., and WILLIAMSON, C. S. The experimental production of peptic ulcer. Ann. Surg., 1923, 77: 409.
8. MATHEWS, W. B., and DRAGSTEDT, L. R. The etiology of gastric and duodenal ulcers. Surg., Gynec. & Obst., 1932, 55: 265.
9. MCCANN, J. C. Experimental peptic ulcer. Arch. Surg., 1929, 19: 600.
10. MORTON, C. B. Observations on peptic ulcer. Ann. Surg., 1927, 85: 207, 229, 879.
11. ORNDORFF, J. R., FAULEY, G. B., and IVY, A. C. The prophylactic value of gastric mucin in the therapy of post-operative jejunal ulcer. An experimental study. Am. J. Digest. Dis. & Nut., 1936, 3: 26.
12. SEELY, H., and TOLLINGER, R. Fundusectomy in the treatment of peptic ulcer. Surg., Gynec. & Obst., 1935, 61: 155.

ENDOMETRIAL HISTOLOGY AND PATHOLOGY AS REVEALED BY THE BIOPSY METHOD[1]

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THE modern interpretation of the cyclic changes in the endometrium dates from the work of Hitschmann and Adler in 1908. Prior to that time the efforts of students of the endometrium had generally been directed toward describing a single norm for the appearance of the endometrium between the menstrual periods. All deviations from that alleged norm were considered pathological. The classical discoveries of Hitschmann and Adler have been confirmed and extended by numerous investigators. Noteworthy among recent discussions of the subject are those by Schroeder, Novak (11), Herrell and Broders, and Bartelmez and Bensley (2).

Two recent advances, however, seem to us to call for a new description of the endometrial cycle. The first of these is the isolation of the hormones of the graafian follicle and corpus luteum, and the demonstration that they are capable of reproducing all the phases of the normal menstrual cycle, either in the castrated monkey (Hisaw) or in the castrated human female (Kaufmann, Clauberg, and Neustaedter). With these observations at hand we are not forced to limit ourselves to a morphological description of the changes taking place in the endometrium, but may interpret these changes in terms of physiological processes.

The second advance is the development of methods for obtaining biopsies from the endometrium by Klingler and Burch, Hoffmann, Novak, Randall, and others. The older descriptions of the endometrial cycle were based upon the study of tissue obtained by autopsy, hysterectomy, or curettage. Such material is subject to two disadvantages: In the first place, autopsy and hysterectomy specimens are likely to be complicated with pathological changes. In the second place only one autopsy or hysterectomy specimen can be obtained from any patient, and only a single curettage specimen can be obtained from any one cycle. The investigator, therefore, was forced to arrange the various histological pictures which he obtained into a continuous record simply upon the basis of their date in the menstrual cycle. When one considers the variability in the length of various cycles even in the same woman, the difficulties of this procedure become evident. With the endometrial biopsy instrument, however, one may take numerous specimens at short intervals throughout the same cycle, and accordingly may define the succession of events with a precision hitherto impossible. The present article is based upon the study of specimens from more than five hundred endometrial biopsies, of which more than a hundred were treated with various special stains, chiefly the stains for mucin, glycogen, and the Golgi apparatus. The biopsies were secured with the punch instrument designed by Burch.

TERMINOLOGY

Following Hitschmann and Adler, the earlier writers classified the state of the endometrium between the menses into the postmenstrual, interval, and premenstrual phases. This terminology persists even in the recent writings of Novak. The three-fold division, however, does not correspond to our present knowledge of the functional stages of the endometrium; and, the term "resting stage" which has been widely used as a synonym for "interval," is an unfortunate misnomer. Present day writers, accordingly, have tended to divide the entire cycle into a stage of tissue loss (comprising the first 1 or 2 days of bleeding), a stage of re-epithelization (the following 2 days), a proliferative or pre-ovulatory stage (lasting about 10 to 12 days), and a secretory or postovulatory stage (lasting 12 to 14 days). The words "proliferative" and "secretory" are accurate descriptive terms, and are highly satisfactory in describing the

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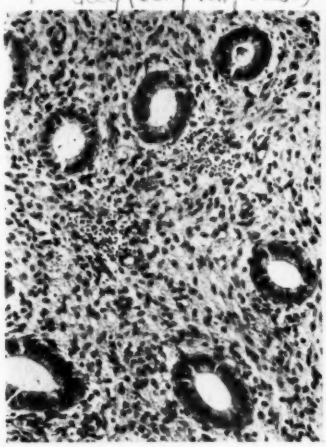
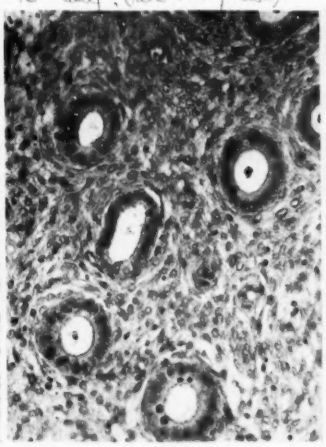


Fig. 1.



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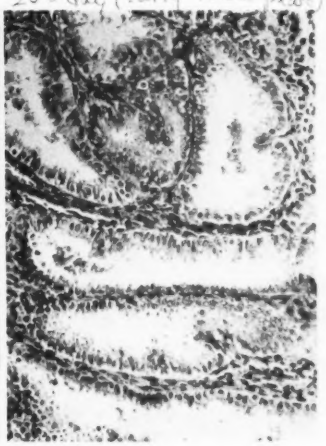


Fig. 3.

Fig. 1. Endometrial biopsy specimen from a normal woman, taken on the ninth day of the cycle. The picture is typical of the early follicular phase. ×140.

Fig. 2. Specimen from the same patient as the previous figure, taken on the sixteenth day of the same cycle. The follicular effect is fully developed. Ovulation probably occurred at about this time. ×140.

Fig. 3. Specimen taken from the same patient as shown in the previous two pictures, taken on the twenty-third day of the same cycle. In this photomicrograph the luteal effects are now well developed but are still fairly early as is evidenced by the presence in some places of a clear zone between the gland nuclei and the basement membrane. ×140.

normal cycle. They are inadequate, however, for classifying the abnormal histological pictures which result from a deficiency or excess of follicular or corpus luteum hormone stimulation. We have accordingly given up (though not without some reluctance) the morphological terminology, and prefer to classify the histological findings in the endometrium on the basis of the phase of endocrine activity which produces them. Hence we shall use the expressions "follicular phase" and "luteal phase" in place of "proliferative" and "secretory."

MENSTRUATION AND RE-EPITHELIZATION

Women are wont to call any kind of vaginal bleeding "menstruation." Unfortunately, the term is also well established in medical nomenclature to designate two very different processes. The first of these, the bleeding which follows the regression of a normal corpus luteum, must be considered the normal menstruation of the human female. The second form of bleeding, which does not come from a luteal type of endometrium is often referred to as "anovulatory menstruation." The two processes are very different both from a histological and from a physiological viewpoint, as will presently be pointed out. Though it is probably too late to change the established terminology, it is obvious that much confusion could be avoided if the term menstruation could be limited to the normal menstrual flow, and the term "follicular bleeding" could be applied to the bleeding which occurs without ovulation.

For our present detailed knowledge of the endometrial changes which occur during normal menstruation we are largely indebted to Bartelmez (1). The premenstrual congestion and leucocytic infiltration are followed by extravasation of blood into the tissues. The endometrial glands lose their secretion and collapse. Bleeding by rhexis from both arteries and veins follows, with destruction of the capillary bed. The tissue loss which results, involving the compacta and most of the spongiosa, is characteristic of normal menstruation, or as Bartelmez terms it, "menstruation following pseudopregnancy." Bartelmez believes that the extravasation, destruction of the capillary bed, and the leu-

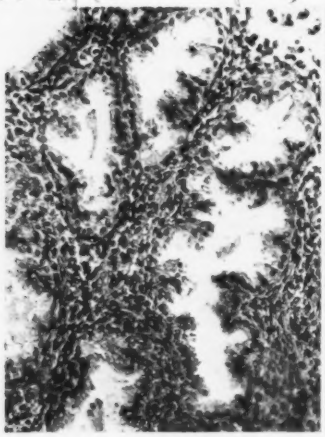
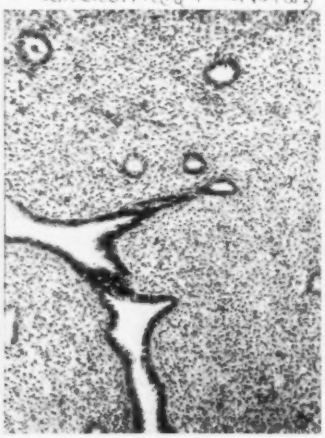


Fig. 4.



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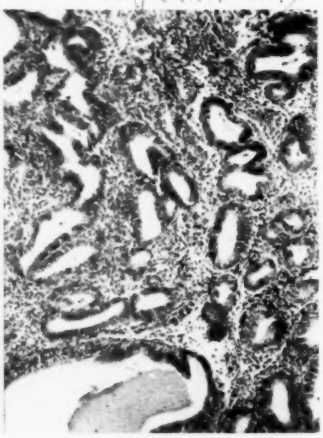


Fig. 6.

Fig. 4. Specimen from the same patient as the previous three pictures, taken on the thirtieth day of the same cycle. The disappearance of the basal clear zone and the increased irregularity of the gland lumens indicate a late luteal phase. Menstruation began following day. ×140.

Fig. 5. Biopsy specimen from a woman 20 years old who had suffered from amenorrhea for 2 years. The opening in the center of the field is a fold of the endometrial surface. The specimen approaches the picture found in castration except that the stroma is not as dense as in complete castration. ×63.

Fig. 6. Specimen from endometrium from a woman 26 years of age who had been suffering from amenorrhea for 6 years. The picture is not at all that of castration, but rather that of the follicular phase with more irregularity and dilatation of the glands than normal. ×63

cocytosis are responsible for the disintegration and shedding of tissue. Sections of the endometrium at the end of the period of tissue loss have all the appearance of sections from a freshly curetted uterus.

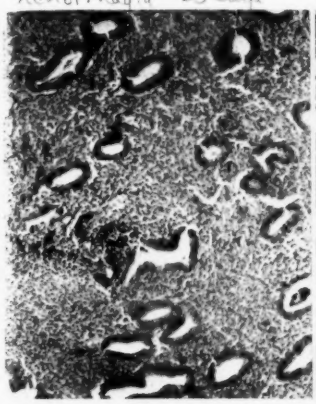
The stage of tissue loss is brief, lasting not more than 1 or 2 days. Before it is completed re-epithelization has already been begun by growth of the epithelium from the remaining portions of the glands. As Herrell and Broders point out, mitotic figures are infrequent during this stage of re-epithelization. The process is independent of endocrine control, and will take place even if castration has been performed immediately before menstruation. At the end of this stage microscopic sections reveal a thin endometrium with infrequent small straight non-secreting glands.

THE FOLLICULAR (PROLIFERATIVE) PHASE

The next stage of endometrial activity is a response to the hormones secreted by the newly developing graafian follicle. Its characteristic feature is cellular proliferation, which is indicated by the presence of numerous mitotic figures in the stroma and especially in the glandular epithelium. The endometrium increases in thickness and vascularity, and both stromal and glandular cells increase in size. Most of the nuclei in the glands remain in contact with the base of the cells. The Golgi apparatus is seen as a conspicuous skein lying between the nucleus and the luminal end of the cell. No glycogen or mucin is present. Many of the epithelial cells are ciliated. The lumens of the glands are round and regular. The thin albuminous secretion which is present seems simply to ooze from the cells. Early in the follicular phase the stroma or interstitial tissue is very loose, and is suggestive of embryonal connective tissue. Later, the stroma is observed to become progressively more dense and less fibrillar. Toward the end of the follicular phase the proliferation becomes much slower, mitotic figures are fewer, and the glands present a somewhat wavy form upon longitudinal section, but are never definitely coiled.

THE LUTEAL (SECRETORY) PHASE

Very soon after ovulation the hormone of the corpus luteum (progestin, corporin, or



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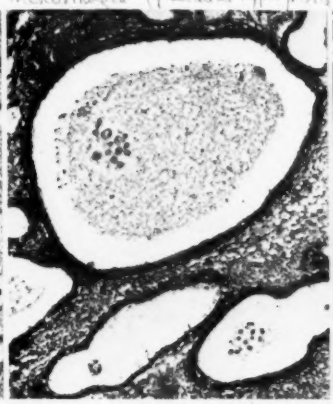

Fig. 8.

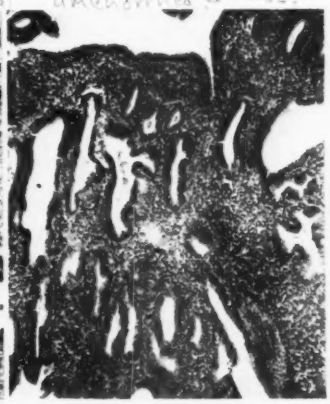

Fig. 9.

Fig. 7. Specimen of endometrium from a woman 36 years old suffering from menorrhagia. This specimen which was taken during the twenty-third day of continuous flow, shows no resemblance to the classical "Swiss cheese" picture. Rather it is essentially the same as the section shown in the previous figure from a patient suffering with amenorrhea. ×57.

Fig. 8. Endometrium from a 16 year old girl suffering from menorrhagia. The specimen was taken during the thirty-fifth day of flow. We have found this typical Swiss cheese endometrium rather infrequently among our cases of endocrine menorrhagia. Such an endometrium is frequently referred to as "hyperplastic" though the cells lining the retention cysts are actually atrophic. ×57.

Fig. 9. Specimen of endometrium from a 20 year old girl following 3 months of amenorrhea. ×57.

progesterone) begins to manifest its influence upon the endometrium. The first characteristic manifestation is the elevation of the nuclei from the bases of the cells of the glandular epithelium, producing with ordinary stains a conspicuous basal clear zone similar to that which Hisaw has observed as an early corporin effect in the monkey. This striking and specific change, like the other features of corpus luteum activity, begins at the necks of the glands and proceeds toward the deeper portions of the endometrium, but leaves the fundic ends of the glands practically unaffected. Specific stains show that the "clear zone" is filled with masses of glycogen which have pushed the nuclei up toward the lumens of the glands. Other features of the early luteal phase are a rapid reduction in the number of mitotic figures, and an enlargement and pronounced elongation of the cells lining the endometrial glands.

The glycogen masses remain basal in the epithelial cells for only about 2 days, and then begin to migrate to the luminal ends of the cells. Special stains then show the glycogen massed in club-like protrusions of the cells extending into the lumens of the glands. Ordinary routine staining methods, in which the glycogen is dissolved out of the tissue, give the impression of a fraying of the luminal ends of the cells. The glycogen is gradually secreted into the endometrial glands. Mucin makes its appearance later than glycogen. The substance which takes the specific mucin stains is found only in the lumen of the gland and never in secretory cells. Fat globules do not normally occur in the cells or their secretion. During the period of active secretion the Golgi skeins become somewhat larger and coarser, but do not change markedly in structure or position.

The cytological changes which we have described result in a conspicuous alteration in the structure of the endometrium. Though the whole endometrium becomes thicker during the period of luteal activity, the thickening does not keep pace with the increase in the size of the glands which results from enlargement of the secreting cells and dilatation of the glands with secretion. In consequence the glands become coiled and tortuous. The enlargement of secretory cells and resultant crowding is responsible for tuft-like protrusions of the cells into the gland lumen. The lumen of such a gland exhibits on longitudinal section a typical "saw tooth" appearance.

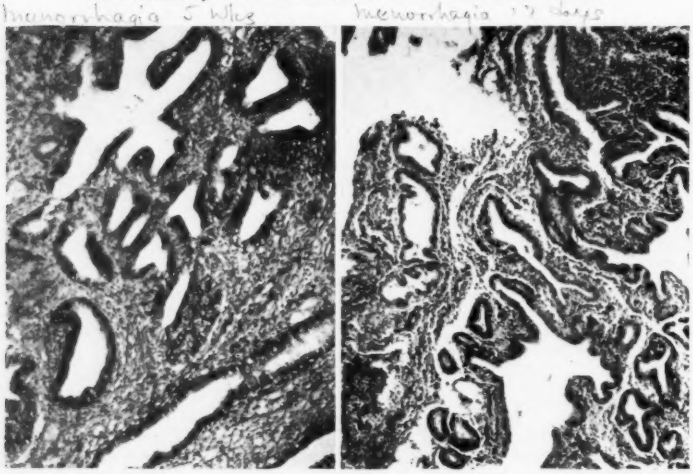

Fig. 10. Fig. 11.

Fig. 10, left. Specimen of endometrium from a 16 year old girl, taken after 5 weeks of menorrhagia. ×65.

Fig. 11. Specimen of endometrium from a 16 year old girl suffering from menorrhagia. Taken on the seventeenth day of flow. ×65.

Coiling of the glands is most noticeable in the middle layers of the endometrium. Here their tortuosity becomes so great that the stroma cells are crowded out and are forced up toward the surface of the endometrium. This process divides the endometrium into three distinct zones. The superficial zone (zona compacta) is composed of relatively straight glands separated by masses of stroma cells. The middle zone (zona spongiosa) is composed of many coiled glands with hardly any interstitial cells between. The deepest layer of the endometrium (zona basalis), as has been mentioned, is only slightly affected by the cyclic changes.

The endometrium in the stage of fully developed luteal activity is frequently diagnosed as "endometrial hyperplasia," or, even more unfortunately, "hyperplastic endometritis." It should hardly be necessary to point out that these terms are absolutely unjustified, for it has been amply demonstrated ever since the work of Hitschmann and Adler that this histological picture is not pathological but is a phase of the normal endometrial cycle.

Late in the luteal phase further changes occur. The columnar cells which line the endometrial glands have now discharged most of their glycogen and appear shrunken. The lumens of the glands become even more ragged in outline. The endometrial arterioles assume a definitely spiral shape. The stroma cells of the compacta, which have been gradually increasing in size now become definitely edematous. The stroma cells have by this time entirely lost their fibrillar character, and their polygonal cell walls may now be definitely seen. The interstitial tissue at this stage sometimes receives the designation "decidua menstrualis." This term is unfortunate, because the presence of glycogen in the stroma cells, which is the characteristic feature of true decidua, is not observed. Finally congestion and leucocytic infiltration herald the next menstrual period.

THE FUNCTIONAL PATHOLOGY OF THE ENDOMETRIUM

The endometrial biopsy punch is obviously liable to miss a small area of carcinoma, if such be present in the uterus. *Biopsy should never be accepted as a substitute for curettage when a neoplasm is suspected.* On the other hand the minimal disturbance to the patient occasioned by the taking of an endometrial biopsy, and the possibility of obtaining sev-

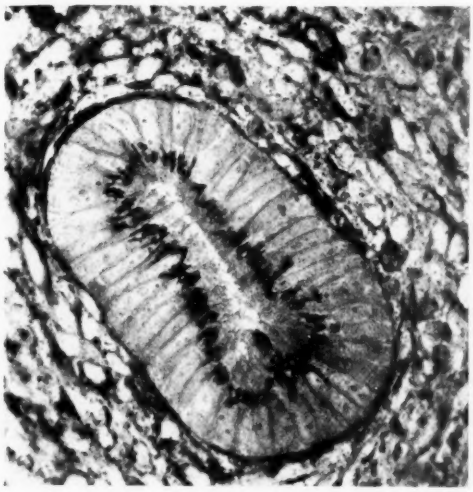

Fig. 12. Gland from endometrium in follicular phase stained to show Golgi apparatus. ×600.

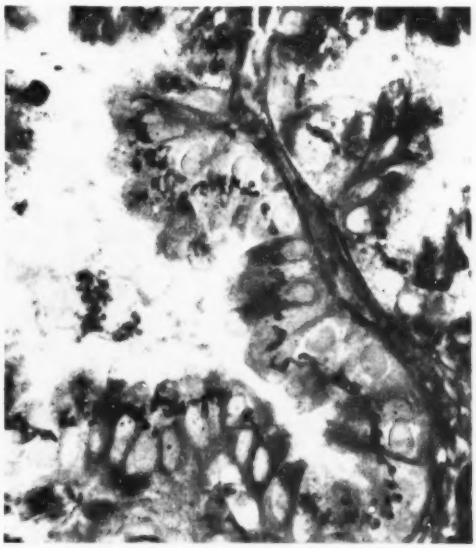

Fig. 13. Endometrium in luteal phase, stained to show Golgi apparatus. ×600.

eral endometrial specimens during a single cycle, make this a very useful procedure in determining what endocrine disturbance, if any, may be the cause of such a condition as amenorrhea, menorrhagia, or sterility.

A. *Abnormalities of luteal function.* Maturation of a graafian follicle and ovulation are necessary antecedents to the formation of a normal corpus luteum. Accordingly, though luteinization may be disturbed while follicular development is normal, follicular function can hardly be disordered without gravely interfering with ovulation and luteinization. In the interest of simplicity, therefore, we shall invert the logical order, and shall describe first the abnormalities of luteal function, and afterward the abnormalities of follicular function.

Three functional disorders of the corpus luteum have been described: (1) failure of luteinization, (2) excessively prolonged luteal activity, and (3) an abnormal secretion producing a so called "mixed picture" in the endometrium. Failure of ovulation and of corpus luteum formation is by all odds the commonest and most important of these conditions. It is easily diagnosed by the absence of the luteal type of endometrium before an expected bleeding; this luteal reaction should occur 4 weeks following the onset of the previous menstrual period. Excessively prolonged luteal secretion is theoretically possible with such conditions as corpus luteum cysts. Herrell and Broders have made the diagnosis of prolonged corpus luteum activity but their evidence is not conclusive. We have not been confronted with this condition. As far as we can judge from our observations, the part of the cycle with variable duration appears to be the follicular phase. Once a corpus luteum has formed it appears to run its course with great uniformity and to regress after not more than fourteen days, precipitating the next menstrual flow. Regarding the so called "mixed picture," we are also inclined to be skeptical. A biopsy taken early in the luteal phase may show manifestations of luteal activity near the necks of the glands, and deeper in the endometrium show only glands typical of the follicular phase, but this is a normal phenomenon. Corpus luteum formation appears to us to be a very constant "all-or-none" reaction, and in case a corpus luteum is formed, it is apparently able almost invariably to override the effects of the estrogenic hormone which is normally secreted at

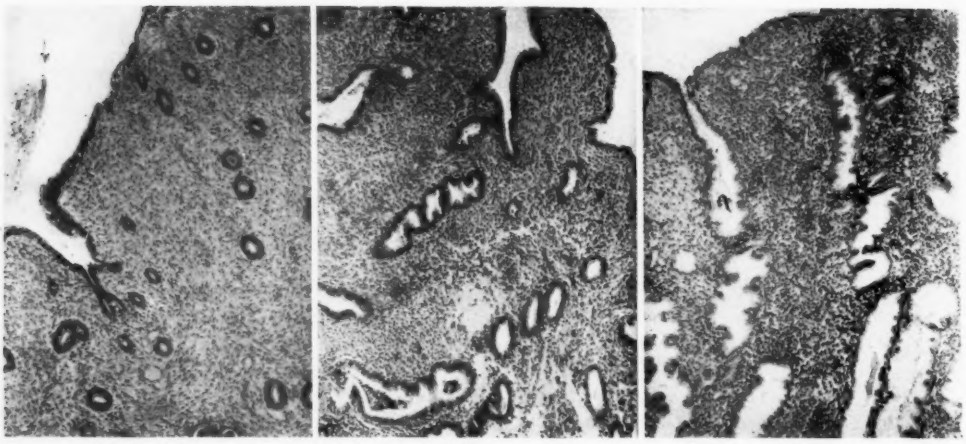

Fig. 14 Fig. 15. Fig. 16.

Fig. 14. Specimen from normal woman, thirteenth day of cycle showing follicular type of endometrium. ×57.

Fig. 15. Specimen from same patient as previous picture, taken on twentieth day of the same cycle. Early luteal effects. ×57.

Fig. 16. This specimen is from the same patient as shown in the previous photomicrographs and was obtained on the twenty-seventh day of the same cycle. The specimen is a good example of the fully developed luteal stage. ×57.

the same time. The question of a mixed picture has arisen only a few times in over five hundred biopsies, and we have never made the diagnosis without grave doubts.

B. *Abnormalities of follicular functions.* In cases in which there is a failure of corpus luteum formation a variety of disorders of follicular secretion may also be manifested in the endometrium. The simplest case is that of castration. In this condition the endometrium is scanty, the stroma very dense, and the glands small and infrequent. Mitotic figures are absent. The cells lining the glands are crowded together in such a way that the nuclei appear very narrow and spindle-shaped instead of ovoid. Besides the cases of absolute castration, one finds numerous cases of amenorrhea in which the level of follicular activity is reduced almost to the castrated type. In this group are included many cases of menopause and premature menopause. When follicular activity is not completely absent the endometrium is slightly thicker and the glands appear somewhat more numerous. The glands may be somewhat dilated and retention cysts may even be present.

In contrast to this well defined group including castration and inactivity approaching the castrated state, we are confronted with a large number of cases of amenorrhea, recurrent follicular bleeding, and menorrhagia in which the endometrial histology closely resembles that of the fully developed follicular phase. The three conditions cannot be distinguished from one another by any difference in their endometrial histology. In the case of recurrent follicular bleeding and menorrhagia it is interesting to observe that in contrast to normal menstruation bleeding occurs from a follicular type of endometrium and also occurs without loss of tissue. Even the bleeding points generally cannot be made out. Recurrent follicular bleeding often so closely simulates normal menstruation that it can be distinguished only by a histological examination of the endometrium. In these three clinical conditions, the endometrium may differ from that of the normal follicular phase in three respects: the glands are often more irregular than normal, the lining cells may be pseudostratified, and more or less dilatation of the glands is usually present. Dilatation of the endometrial glands is fairly reliable evidence that prolonged follicular stimulation has taken place without the interruption of luteal activity and normal men-

struation. The glandular dilatation may be found in all degrees up to the typical "Swiss cheese" endometrium. We have found the fully developed Swiss cheese picture rather rarely, and in our material it has been no more characteristic of menorrhagia than of amenorrhea.

The fact that amenorrhea, cyclic follicular bleeding, and menorrhagia of the endocrine type may be indistinguishable on the basis of endometrial histology is worthy of repetition. The endometrial biopsy is evidently not yet an adequate substitute for a good clinical history.

SUMMARY

It is the purpose of this paper to point out the characteristic manifestations produced in the endometrium by the follicular and corpus luteum hormones, and to recommend the examination of the endometrial histology by the biopsy method as a control for endocrine diagnosis and therapy. *Up to the present time the physiological changes of the normal endometrium have not been sufficiently appreciated by the clinician or even by the clinical pathologist.*

BIBLIOGRAPHY

1. BARTELMEZ, G. W. Histological studies on the menstruating mucous membrane of the human uterus. Contributions to Embryology, Carnegie Institute of Washington, No. 142. 1933, 24: 141–186.
2. BARTELMEZ, G. W., and BENSLEY, C. M. Human uterine gland cells. In: Special Cytology, Vol. 3, Chap. 38, 1523–1564. By E. Cowdry. New York: Paul B. Hoeber, 1932.
3. CLAUBERG, C. Die Wirksamkeit des Luteohormons, des spezifischen Hormons des Corpus luteum, am menschlichen Uterus. Zentralbl. f. Gynaek., 1932, 56: 2460–2463.
4. HERRELL, W. E., and BRODERS, A. C. Histological studies of endometrium during various phases of menstrual cycle. Surg., Gynec. & Obst., 1935, 61: 751–764.
5. HISAW, F. L. The physiology of menstruation in Macacus rhesus monkeys; influence of follicular and corpus luteum hormones; effects of anterior pituitary extracts. Am. J. Obst. & Gynec., 1935, 29: 638–659.
6. HITSCHMANN, F., and ADLER, L. Der Bau der Uterusschleimhaut des geschlechtsreifen Weibes mit besonderer Berueecksichtigung der Menstruation. Monatschr. f. Geburtsh. u. Gynaek., 1908, 27:1–82
7. HOFFMANN, P. Biopsy specimens of the endometrium. Am. J. Obst. & Gynec., 1934, 27: 616–618.
8. KAUFMANN, C. Umwandung der Uterusschleimhaut einer kastrierten Frau aus den atrophischen Stadium in das der sekretorischen Funktion durch Ovarialhormone. Zentralbl. f. Gynaek, 1932, 50: 2058–2061
9. KLINGLER, H., and BURCH, J. Suction in obtaining endometrial biopsies. J. Am. M. Ass., 1932, 99:559–560.
10. NEUSTAEDTER, T. The production of active endometrium in the human castrate. Am. J. Obst. & Gynec., 1935, 29:680–685.
11. NOVAK, E. Cyclical changes in the genital canal. In: Obstetrics and Gynecology, vol. 1, 306–326. By A. Curtis. Philadelphia: W. B. Saunders Co., 1933.
12. Idem. Suction-curet apparatus for endometrial biopsy. J. Am. M. Ass., 1935, 104: 1497–1498.
13. RANDALL, L. M. Endometrial biopsy. Proc. Staff Meet., Mayo Clin., 1935, 10:143–144.
14. SCHROEDER, R. Der mensuelle Genitalzyklus des Weibes und seine Stoerung. In: Handbuch der Gynaekologie, vol. 1, part 2, 551. By J. Veit and W. Stoeckel. Muenchen: J. F. Bergman, 1928.
15. Idem. Die Weiblichen Genitalorgane. In: Handbuch der mikroskopischen Anatomie des Menschen, vol. 7, part 1, 329–356. By W. Moellendorff. Berlin: Julius Springer, 1930.

"ACUTE" SUBDURAL HEMATOMA AND ACUTE EPIDURAL HEMORRHAGE[1]

A Study of Seventy-two Cases of Hematoma and Seventeen Cases of Hemorrhage

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Acute Subdural Hematoma

We here present 72 cases of "acute" subdural hematoma diagnosed at either operation or postmortem examination from 24 hours to 21 days after head injury. Cases of head injury dating back longer than 3 weeks were excluded.

Virchow described this condition in 1857. He pointed out that in the insane, in the chronic alcoholic, and in the luetic, there occurred a subdural inflammatory process which he termed pachymeningitis hemorrhagica interna. Since that time much has been learned.

Trauma is the most frequent cause of subdural hematoma, usually mild in chronic cases with the development of signs or symptoms months or years later. In the "acute" hematoma, the type under discussion, however, the injury is usually, although not necessarily, severe and the underlying brain almost never escapes damage. In the acute period unconsciousness and a bloody spinal fluid are usually present. While trauma is the most frequent cause, there is no doubt that alcoholism, syphilis, various abnormal conditions of the blood and blood-forming organs (anemia, leucemia, scurvy, avitaminosis) and brain tumors which interfere with the dural venous drainage are predisposing factors to such an accident. In children birth trauma, syphilis, malnutrition, scurvy, and the acute exanthemas have all been described as predisposing factors. Studdiford has recently pointed out that subdural hematomas are most likely to occur in newborn infants obstetrically ill-born.

In describing his four cases of chronic subdural hematoma Trotter pointed out that these lesions usually follow a slight trauma which is received in the anteroposterior diameter and that the blood which enters the subdural space is due to the rupture of a cerebral vein as it bridges that space en route to the longitudinal or lateral sinuses. The underlying brain is usually undamaged. Only rarely is there an associated fracture of the skull. The "acute" subdural hematomas, on the other hand (Vance, Apfelbach, Leary), are more often, though rarely, associated with skull fracture (usually lateral or posterior) and almost invariably associated with an underlying brain laceration and rupture of a cerebral cortical vein. Subdural hematomas may also result from a tear in one of the dural sinuses. These occur usually with fractures or penetrating wounds. Occasionally, subdural bleeding follows an epidural hemorrhage in which the dura has been lacerated and epidural blood enters the subdural space. Rarely this type of hemorrhage may occur without trauma. Helpern has recently reported such a case in which a cerebral aneurism ruptured at the point where the internal carotid passes through the subdural into the subarachnoid space to continue as the left middle cerebral artery.

Once blood enters the subdural space, however, its further course is the same whatever the original etiology may be. The acute hematomas manifest themselves clinically at a much earlier date because there is so much associated brain damage. These lesions all start as a collection of blood and cerebrospinal fluid caught in a space from which little absorption occurs. The attempt which the body makes to organize and remove this clot is the work of the dura. Within several hours after the receipt of the injury the fibrovascular layer which eventually envelops the blood has already begun to form. It is usually fairly complete in a matter of two to three weeks. As has been said by Merritt and Munro, this admixture may become either a completely solid clot or a collection of cerebrospinal fluid with high pro-

[1] From the Neurological and Neurosurgical Departments, Bellevue Hospital, New York; read at the meeting of the American Neurological Association, Atlantic City, New Jersey, June, 1936.

tein content. They point out that those intermediate clots possessing any especial degree of fluidity are probably expanding lesions. That they do increase in volume is evident from their clinical course. The following factors may contribute:

1. Gardner has shown that the clot having been formed and the membrane organized, that portion of the membrane adjacent to the arachnoid may act as a semi-permeable membrane through which the cerebrospinal fluid passes into the subdural space. This is an attempt to equalize the differential osmotic tension between the fluid in the subarachnoid space and the highly concentrated protein fluid (blood) in the subdural space.

2. Putnam, Zollinger, and Gross have shown that there occurs a gradual disintegration of the encysted red blood cells with the resultant liberation of hemoglobin from the cell stroma and its reduction to smaller protein aggregates. This produces a higher effective osmotic pressure. They believe that the substance added to the hematoma to increase its volume must come, at least in part, from the plasma of the circulating blood. The large dilated capillaries in the outer wall of the hematoma sac usually lie close to the lumen of the cyst. An exchange of fluids between the two is therefore probable.

3. Rupture of the dilated capillaries seen in the outer wall of the hematoma sac adds blood to its contents.

4. Repeated bleeding may come from the original source of hemorrhage.

It is probable that in most cases more than one factor exists. One type of subdural fluid collection warrants comment. In 1924 Naffziger described abnormal collections of cerebrospinal fluid in the subdural space following trauma under the name of subdural hydroma. He pointed out that since no normal connection existed between the subdural and subarachnoid spaces it was necessary to assume a tear in the arachnoid at the time of the trauma allowing cerebrospinal fluid to enter the subdural space.

DIAGNOSIS

Subdural hematomas follow about 9 to 13 per cent of all severe head injuries. These figures are appalling when we realize how seldom this condition is diagnosed clinically. The diagnosis of the chronic type of subdural hematoma has been discussed often and its difficulties stated. It is usually confused with brain tumor, post-traumatic neurosis, lues, or vascular accident, and is often disclosed only at operation or at the autopsy table. Dyke has recently described in one case what he considers to be a typical encephalographic sign of chronic subdural hematoma. He was able to demonstrate a collection of air in the subdural space which appeared to be surrounding a mass and was able to make a diagnosis of subdural hematoma prior to operation. His case is, however, very unusual and of uncertain practical importance, since air injected by the lumbar route does not usually enter the subdural space unless an abnormal communication with the subarachnoid space exists. In addition, this procedure is of value only in the chronic hematoma. The "acute" subdural hematoma patients are much too ill to permit of such a diagnostic procedure. In infants the condition is usually mistaken for hydrocephalus, birth injury, brain tumor, or some congenital abnormality. Suspicion should be aroused by any infant with progressive enlargement of the head, changes in the optic fundus and signs of brain involvement (usually convulsions or hemiparesis). The diagnosis may be confirmed by puncturing the fontanel. Bloody fluid will be obtained as soon as the membranous fontanel is pierced.

The diagnosis of "acute" subdural hematoma is equally difficult. Those patients who are admitted to the hospital with a head trauma are immediately put on a dehydration regimen. The following are especially significant: (1) The *development* of focal signs usually of a hemiparetic nature or the progression of those focal signs which may already exist at the time of admission; (2) "in and out" consciousness or progressive stupor; (3) a pulse rate below 60; (4) the sign of the dilated pupil has been in our experience a very valuable localizing sign. In the event of operation, the first trephine opening should always be on the side of the dilated pupil.

The spinal fluid in these cases on admission is usually bloody although it may be xantho-

chromic or even clear. While of no value in making the definite diagnosis of subdural hematoma, lumbar puncture should be performed in these cases because the type of spinal fluid indicates roughly the prognosis of any given case of head trauma. In addition, the withdrawal of spinal fluid by lumbar puncture allows an equal amount of blood to enter the cranial cavity and thereby help in the repair of injured brain tissue. This fundamental concept of brain surgery was introduced by Dr. Temple Fay and is probably the most important factor in keeping his mortality rate for head injury so low.

THERAPY

All patients with head trauma routinely receive the following treatment until such time as it is to be decided that operative intervention be advisable:

1. Shock if present is treated with intravenous injections of hypertonic glucose solution (from 100 to 150 cubic centimeters of 50 per cent sterile dextrose). Morphine is denied and instead one of the barbital derivatives is used.

2. Lumbar puncture is performed.

3. Hypertonic dextrose solution is administered repeatedly by vein for brain dehydration (100 cubic centimeters of 50 per cent sterile dextrose three times daily). Evidence has recently been advanced to indicate sucrose, a disaccharide, is a superior dehydrating agent; it is not stored but is entirely eliminated by the kidneys. We are experimenting with this drug at the present time.

4. Caffeine sodiobenzoate is given by hypodermic injection (7½ grains every 4 hours).

5. By means of rectal drip, from 90 to 120 cubic centimeters of 25 per cent dextrose solution is given every 4 hours.

6. The head of the bed is elevated 15 to 45 degrees.

In discussing the further therapy of subdural hematoma, it must be emphasized that the only method for the removal of blood in the subdural space is its surgical evacuation: it possesses practically no capacity to rid itself of any quantity of entrapped blood. The operative approach to these lesions utilizes one of three methods: (1) the osteoplastic flap; (2) the subtemporal decompression with associated clot removal; and (3) the bilateral trephine exploration. We greatly prefer the last method and use it in all our cases for the following reasons:

1. It saves time.

2. The operation is done under local novocain anesthesia and is much less shocking than either of the other two methods. Even though the clot be bilateral, this procedure can be carried out without damage to the patient.

3. If the clot is too solid to be removed by suction (a rare occurrence in "acute" subdural hematoma) the trephine opening may be used as a point for the turning down of the bone flap.

4. As will be noted in the statistical study it is often difficult to determine the side of the lesion or indeed the presence of a subdural hematoma. Trephining allows us to expose the subdural space without undue shock to the patient. In the event that these trephines result in a negative exploration, these same openings may be used for ventriculography.

It has been argued that the trephine approach to subdural hematoma results in an incomplete removal of the entrapped blood and that the blood remaining in the subdural space might act as the nucleus for the reformation of another clot. Two cases which came to autopsy (from other causes) several months after the successful but non-total removal of a hematoma through an enlarged trephine opening refute this argument. In both instances there was no sign of any blood in the subdural space and no evidence of any membrane formation although at the time of operation it was known that a small amount of blood had been left in the subdural space.

STATISTICAL SURVEY—SEVENTY-TWO CASES

Of the total number of cases reported, 49 patients were seen by members of the neurological service at Bellevue Hospital with 40 accurately diagnosed. In the past year 27 patients came to our attention with accurate diagnoses in 24 cases. Of the 23 other cases studied 4 were accurately diagnosed; in many the diagnosis had not been suspected.

There were 51 males and 21 females. Sixty-eight were white people and 4 were colored.

As to contributory diseases, acute alcoholism complicated 40 of the 72 cases. Other complicating factors were generalized arteriosclerosis (5 cases); lues (2 cases); and 1 each of epilepsy, prematurity, diabetes, pregnancy, and heroin addiction.

Nature of the trauma. In every case in which a history could be elicited trauma was the precipitating factor. The type of trauma varied from a fall during an alcoholic bout to a kick by a horse. In every instance the injury was severe.

The time interval between trauma and symptoms could be judged accurately in only 36 cases; in the others, patients were either in coma at the time of admission or died following operative intervention without an adequate history being obtained. In 29 there was an immediate loss of consciousness following the trauma; in the others, the time interval varied between several minutes and 15 days.

The initial period of unconsciousness varied from "a few seconds" to 24 hours. Those patients with an initial period of prolonged unconsciousness were much less likely to survive. In 65 of the cases reported there was an immediate loss of consciousness at the time of the accident. To what extent alcoholism contributed cannot be stated with certainty.

The lucid interval varied anywhere from 3 hours to 21 days. Only 3 of our cases had a lucid interval of over 15 days. It can thus be seen that we are dealing with an acute process.

As to *vomiting*, 37 of the 72 patients vomited at some time during their hospital stay.

Specific notes regarding *headache* were made in 41 cases. It was present in 36.

Ten patients had generalized *convulsions* under observation, 4 being of Jacksonian type. These latter, however, proved of no diagnostic aid, for on two occasions the lesion was on the side contralateral to the convulsion and on two occasions it was on the same side.

In 25 cases patients *bled* from nose or ears.

Outward evidences of head trauma were noted in 45 of the 72 cases. Ten other cases had signs of trauma elsewhere on the body.

In 40 patients *incontinence* of urine or feces was noted.

TABLE I.—AGE INCIDENCE

Age in years	Cases
0 to 9	2
10 to 19	3
20 to 29	11
30 to 39	17
40 to 49	16
50 to 59	15
60 to 69	4
70 to 79	4
Total	72

Pupils. In 42 of the 72 cases the pupils were unequal; in 30, the lesion was found on the side of the dilated pupil; in 12, on the side opposite the dilated pupil; in the 30 additional cases the pupils were equal at all times.

Papilledema. The fundi were examined in 54 cases. Twenty had papilledema; 11 had engorgement of the fundal veins; in 23 cases the fundi were normal.

Cranial nerve palsies. In the 50 cases of hemiparesis the lower facial was involved on that side. In addition there were 7 cases of third nerve paralysis and 2 of sixth nerve paralysis; otherwise the cranial nerves escaped injury. However, there are many difficulties associated with testing the cranial nerves of patients with head trauma, and the records must be examined critically.

Motor weakness. Fifty patients showed localizing signs in the nature of a hemiparesis or a hemiplegia: in 20, the lesion was found on the side opposite this motor weakness; in 20 others, on the same side; and in 10, operation or postmortem examination revealed bilateral subdural hematomas. Fourteen patients showed generalized flaccidity; 4, generalized spasticity; and only 4 patients showed no evidence of paresis or paralysis.

These statistics indicate that at operation one should first trephine on the side of the dilated pupil since this is almost three times as accurate a localizing sign as the sidedness of the paralysis which is indeed of but doubtful assistance. However, no sign is unfailing and bilateral trephine is always needed. Ten cases had a dilated pupil and motor weakness on the opposite side. The lesion was found on the side of the dilated pupil in 7 cases.

Sensory examination was found to be of no aid in the diagnosis of subdural hematoma, and for that reason is not included here.

Forty-two of the patients had a *stiff neck* at some time during their stay in the hospital. The earlier the patient was seen the more frequently was it possible to elicit this sign. It was always associated with blood in the spinal fluid.

The *deep reflexes* were of no help in arriving at a diagnosis.

The *superficial reflexes* showed:

	Cases
(1) Abdominals	
Bilaterally absent	53
Absent on one side	11
Bilaterally present	8
(2) Babinski	
Bilateral	38
Unilateral	20
No sign	14

When the Babinski sign was bilateral it was usually more marked on the side of the motor weakness.

Mental state on admission. Comatose patients, 46; stuporous, 12; confused, 5; drowsy, 4; clear, 5. Practically all of the patients showed the typical lapsing "in and out of coma."

Aphasic studies were made in 44 cases: 6 had aphasia: 3 in conjunction with right-sided hematomas (1 of these had a laceration of the left temporal lobe) and 3 in conjunction with left-sided lesions.

LABORATORY FINDINGS

The *white blood count* varied from 4,000 with 54 per cent polymorphonuclears to 25,000 with 88 per cent polymorphonuclears. All but 2 cases showed a polynucleosis and a leucocytosis.

The *spinal fluid* examination showed:

	Operation		No operation	
Type of fluid	Lived	Died	Lived	Died
Bloody	7	14	0	16
Xanthochromic	8	6	0	4
Clear	6	0	0	2
Not done	0	1	0	9

There was a definite correlation between the type of spinal fluid and the prognosis. The patients with frankly bloody spinal fluid had the poorest prognosis; and those with clear fluid recovered in every instance if they were subjected to operation. Bloody fluid usually meant brain laceration or contusion.

The *manometric pressure* readings varied from 40 to 650 millimeters of water. In most patients the spinal fluid pressure was normal.

In three instances a positive *blood Wassermann* was obtained and in one of these the *spinal fluid Wassermann* reaction was positive. We believe lues to be an inconsiderable factor in producing this lesion.

As to *blood pressure* 20 patients had evidences of hypertension during their hospital stay; of this number, 12 died; and of the 8 remaining, 4 showed a postoperative return of their blood pressure to normal levels.

The pre-operative *pulse rate* varied from 42 to 160. In 36 cases there was a drop of the pulse rate to below 60 at some time prior to operation or death.

Respiration was found to be of no diagnostic value.

Pre-operative *temperature* varied from 97 to 106.7 degrees F. Twenty patients with a temperature of above 103 degrees F. were operated on; of this number only 4 lived.

Roentgenograms of the skull were made in 17 cases. Of these, only 3 showed evidences of fracture, and in each instance the hematoma was on the side opposite the fracture. There was a pineal shift in only 1 case.

Only 1 patient had an *encephalogram*. This showed a shift of the ventricular system to the side opposite the lesion with obliteration of the cortical markings on the side of the lesion.

The *hematoma* was found on the right side in 32 cases; on the left side in 30 cases; it was bilateral in 10 cases; and in 1 case it was beneath the tentorium.

The *mortality rate* is given in the following table.

MORTALITY RATE

Operation	Cases	Lived	Died	Mortality rate per cent
Neurological service	32	18	14	43 7
General surgical service	9	2	7	77 7
No operation	31	0	31	100 0

Postmortem findings. Twenty-one patients died after operation; 11 were subjected to postmortem examination. In most instances only the head was examined. Two showed evidences of fractured skull. All had extensive

brain laceration in addition to the subdural hematoma which had been fairly completely removed in all cases but 1. Of the 31 cases proved at postmortem to have subdural hematomas, examination only 5 were uncomplicated; the others were all complicated by brain laceration and intracerebral hemorrhage.[1] In 1 case the hematoma was found to be bilateral and beneath the tentorium. Death was rapid in this case, due probably to medullary compression.

SUMMARY

1. Seventy-two cases of "acute" subdural hematoma were seen at Bellevue Hospital from 1912–1936. Of these, 49 were seen by the neurological service with 40 accurately diagnosed. Of the 23 remaining, 4 were diagnosed aright. Twenty-eight were diagnosed at autopsy.

2. The neurological service operated on 32 of these patients with an operative mortality of 43.7 per cent. The general surgical service operated upon 9 of these patients with a mortality of 77.7 per cent.

3. The various signs and symptoms encountered have been discussed, and an attempt has been made to determine various pre-operative prognostic factors.

4. The treatment of subdural hemorrhage is given.

5. We have given the postmortem findings. They show why diagnosis is so difficult and operative mortality so high.

6. The following differences between "acute" subdural hematoma and epidural hemorrhage to be discussed, are here noted:

"Acute" subdural hematoma occurs at all ages; epidural hemorrhage is more apt to occur in young adult and middle-aged individuals.

An epidural hemorrhage usually occurs on the side of the received trauma; an "acute" subdural hematoma is much more likely to be in the nature of a contrecoup phenomenon.

Epidural hemorrhages are almost invariably associated with an overlying fracture line crossing the middle meningeal groove or one of the cranial venous sinuses. "Acute" subdural hematoma is much more rarely associated with skull fracture, usually posterior or lateral in location, and usually contralateral to the hematoma.

The lucid interval in cases of epidural hemorrhage is usually of shorter duration than is that of "acute" subdural hematoma. Overlapping does occur however.

If paresis results in cases of epidural hemorrhage, it is practically always contralateral; in cases of "acute" subdural hematoma a resultant paresis is just as apt to be ipsilateral. In the latter group we have found the dilated pupil to be about three times as accurate a localizing sign as is the side of the paresis.

Epidural hemorrhage is a much less frequent complication of head trauma than is the "acute" subdural hematoma, the incidence being about 1 to 4.

"Acute" subdural hematomas are much more apt to be bilateral.

The mortality rate following operation in cases of epidural hemorrhage was 54.5 per cent; in cases of "acute" subdural hematoma, as noted above, it was 43.7 per cent.

Acute Epidural Hemorrhage

There is a great discrepancy between the number of cases of epidural hemorrhage recognized clinically and the number remaining undiagnosed until they reach the postmortem table. In our opinion, this is due to the fact that the syndrome of epidural hemorrhage is much too rigid. The lesion is not common. In the 6 year period from 1930 to 1936 we observed 17 cases of epidural hemorrhage at Bellevue Hospital. During this same period we saw four times as many cases of acute subdural hematoma. These latter cases have just been discussed.

Epidural hemorrhage complicates 2 to 5 per cent of all craniocerebral injuries. The fact that medical examiners' statistics usually yield a much higher figure is due to their seeing only autopsy material. Such postmortem records,

[1] Ten had skull fracture and in 8 the fracture line was contralateral to the hematoma.

however, are of great value because they indicate to what extent the complicating factor of epidural hemorrhage disturbs the prognosis in any given case of head trauma.

Epidural hemorrhage usually follows a lateral skull fracture which has lacerated one of the branches of the middle meningeal artery —usually the posterior branch. The vessels may be torn by a local depressed fracture or by a crossing line of fracture. The frequent association of this type of hemorrhagewith a skull fracture should not appear unusual when we realize that the middle meningeal artery lies grooved in the bone throughout its course in the skull. The temporal bone is very thin—a slight blow has sufficient force to fracture it.

The bleeding above the dura, therefore, is usually present on the same side as the injury, although it may also be the result of a contrecoup lesion. This was true in one of our cases. It is necessary to keep this type of hemorrhage in mind no matter in what region the outward evidences of skull fracture be found.

The blood collects between the bone and dura, and as bleeding continues, additional branches of the middle meningeal artery are lacerated as they dip in from the bone toward the dura. This adds to the original hemorrhage and when enough blood has collected, signs of compression of the underlying brain occur, usually in the form of contralateral paralyses or convulsions.

These clots are usually unilateral and over the convexity of the brain, although they may occur at the base, over both cerebral hemispheres or over the cerebellum. They are almost always associated with some degree of underlying brain damage—a fact which is not as yet universally recognized and is vital in determining the prognosis in each case (Munro).

Epidural hemorrhage and middle meningeal hemorrhage are not synonymous terms although they usually occur together. On occasions, hemorrhage above the dura may come from a tear in one of the cranial venous sinuses, laceration of the anterior meningeal artery, bleeding from bony fragments at the point of a depressed fracture, or following the turning down of a bone flap in which hemorrhage had not been properly controlled. Still more rarely, it is the result of severe head injury in which the dura has been lacerated and collections of subdural blood have entered the epidural space.

It has been observed repeatedly that epidural hemorrhage is more likely to occur in people during the prime of life. For this circumstance Vance has given a most satisfactory reason.

> In childhood the bony grooves for the middle meningeal artery are shallow and the dura is easily separated from the skull—hence the artery escapes injury except rarely. In elderly people the grooves deepen, and the dura becomes adherent. Extradural clots are therefore rather infrequent, since the adherent dura prevents excessive hemorrhage. In adults, however, the bony grooves are not so deep and the dura is sufficiently adherent to allow laceration of the artery, but not to such an extent as to prevent separation from the bone by the violence.

DIAGNOSIS

The "typical" epidural hemorrhage syndrome is too well known to be repeated here, suffice it to say that one seldom encounters it. But if the so called pathognomonic succession of events is noted, operation should take place at once. Much has been written about the clear spinal fluid which is associated with epidural hemorrhage. However, a word of warning is necessary. While it is true that there is no reason for a pure epidural clot to stain the subarachnoid fluid, the associated brain damage is almost always severe enough to give a "pink" or "bloody" tap. Our general feeling about this type of bleeding is that operative intervention should be undertaken in any case of head trauma with a relapse into a clouded state of consciousness, with a pulse drop to below 60, or where signs of a focal nature (hemiparesis, convulsions) occur tardily or a progression of those focal signs noted on admission. If there be further corroborative evidence in the nature of a fracture line crossing the middle meningeal groove or one of the cranial venous sinuses, operation is imperative. The presence of a dilated pupil should guide the surgeon to the side of the first trephine opening. By adhering to these simple principles we were able to advise operation in 15 of the 17

cases which came to our attention. Yet the diagnosis of epidural hemorrhage or "acute" subdural hematoma does not rest exclusively on these signs. Each case remains a distinct clinical problem, but an analysis of these cases proved these signs to be most helpful in arriving at a diagnosis. Intervention should consist in enlargement of the trephine opening placed midway between ear and vertex large enough to: (1) remove the clot; (2) identify the bleeding point and control hemorrhage; (3) open the dura to search for associated subdural hematoma and produce a better decompression. After operation these patients should have a blood transfusion.

Epidural hemorrhages which follow the turning down of a bone flap are an infrequent occurrence. Once diagnosed their treatment is exactly the same as for any other type. Their prevention is a matter which has as yet not received sufficient attention. Poppin has recently devised an ingenious method for the turning down of a craniotomy flap in which the dura is sutured to the bone in such a manner as to make it practically impossible for epidural clots of clinical importance to form.

STATISTICAL SURVEY—REVIEW OF SEVENTEEN CASES

As to *sex* incidence, there were 14 men and 3 women.

As to *age* 13 of the 17 cases were in the young adult and middle-aged groups emphasized by Vance.

Diagnosis. Ten cases were clinically diagnosed as epidural hemorrhage. Two were diagnosed in the same way as extracerebral (epidural or subdural) hematoma. Three were diagnosed as subdural hematoma, and the epidural hemorrhage was found during the course of the exploration; 2 were not diagnosed during life but were discovered at autopsy. One patient died shortly after examination, and opinions were divided between epidural hemorrhage and tuberculous meningitis. Postmortem examination revealed a huge right epidural hemorrhage weighing 140 grams and no underlying brain involvement. This patient could probably have been saved by operation. In another case a diagnosis of a pontine hemorrhage was made and postmortem examination confirmed this suspicion but there was an associated left epidural hemorrhage weighing about 95 grams.

Nature of trauma. The types of trauma varied: (1) fall, 6 patients—5 of these falls occurred in alcoholic persons, the other during an epileptic convulsion; (2) blow, 5 patients; (3) automobile accident, 2 patients; (4) operative trauma following the turning down of an osteoplastic flap, 1 patient; (5) unknown, 3 patients.

As to *contributory diseases*, alcoholism complicated the picture in 6 patients; generalized arteriosclerosis in 2; hypertensive heart disease with associated renal damage in 1; and epilepsy in another. The 4 latter patients died.

The *time between trauma and onset of symptoms* varied as follows: There was an immediate loss of consciousness in all but one. This primary period of unconsciousness varied from "a second" to 8 hours. Two patients with a prolonged period of primary unconsciousness (7 and 8 hours) died. At postmortem examination both of these patients were found to have sustained severe brain lacerations.

The *lucid interval* is usually defined as that period of relatively clear consciousness which comes between the initial unconsciousness and the final clouding of consciousness, which occurs when enough blood has accumulated between bone and dura to compress the underlying brain. Fifteen of the 17 patients had a lucid interval—this varied in time from 1 hour to 9 days. Two patients never recovered consciousness following the initial trauma; both died. Three patients with a lucid interval of over 4 days (4, 5, and 9 days) all recovered. These facts would seem to show that, when the bleeding is not so rapid as to overwhelm the cerebral compensatory mechanisms, some form of readjustment can be reached, and that with proper operative therapy these patients usually recover.

Of 13, in whom a partial or a complete history could be obtained, 11 complained of *headache.*

In 5 patients *convulsions* were observed. In

2, the convulsions were Jacksonian in nature and were limited to the side opposite the lesion; in the 3 other patients, the convulsions were generalized.

In 4 patients there was *bleeding from external orifices*; 3 from the nose and 1 from the ears.

On admission 14 patients had *visible evidences of head trauma*. In 10 this was on the side of the lesion; in 2, contralateral; and in 2 others there was bilateral evidence of head trauma. These findings are of importance; for epidural hemorrhage nearly always occurs on the side of the trauma, whereas "acute" subdural hematoma usually is found contralateral to the trauma.

In 11 *incontinence* of urine and feces was noted.

Pupils. In 7 of the 17 patients epidural hemorrhage was on the side of the dilated pupil; in 4 cases the lesion was on the side opposite the dilated pupil; and in 6, the pupils were equal.

Vision. One patient had a right homonymous hemianopsia. Here a fracture of the left occipital bone was found postmortem which had torn the posterior branch of the middle meningeal artery, thereby causing an epidural clot. There was also a laceration of the occipital lobe, undoubtedly, the cause of the visual field defect.

Papilledema. The fundi were seen in 16 cases. The remaining fundus was invisible because of myosis and our refusal to use mydriatics lest pupillary evidence would be lost. Four had papilledema; 5 had engorged veins; and in the 7 others, the fundi were found to be normal. The absence of papilledema should not militate against operative interference.

Motor phenomena. (1) Hemiparesis was the most constant motor abnormality. It occurred in 13 cases; in all but 1, the clot was found on the side opposite the lesion. This is in contradistinction to acute subdural hematoma in which the hemiparesis, if present, is just as likely to be ipsilateral.

2. Hemiplegia occurred in 4 cases; always opposite to the clot. Two of the patients had a hemiplegia on admission, the 2 others progressed from a hemiparesis to a hemiplegia under observation. All 4 died. Postmortem examination was performed on 2 of these patients and both showed the presence of brain laceration in addition to the epidural hemorrhage.

3. Generalized rigidity was noted in 1 patient who died.

4. Generalized flaccidity was noted in 1 patient who recovered.

Sensation. No accurate observations could be made on sensation. Sensory examination in patients with head trauma is notoriously inaccurate and usually it is of little assistance in making a diagnosis of epidural hemorrhage.

Reflexes. (1) As to deep reflexes, these findings were of no diagnostic value and for the most part depended on the patient's state of consciousness disappearing entirely when coma set in.

(2) As to superficial reflexes, there was a disturbance in the abdominal reflexes in all. In 15, they were absent bilaterally and in only 2 cases were they absent only on the side opposite the lesion. In like manner all had alteration in the plantar responses. In 12 instances there was a bilateral Babinski sign, usually more marked on the side opposite the lesion; in 5 cases it occurred only contralateral to the lesion.

Mental state. All those patients who had had a lucid interval showed a progressive clouding of consciousness. The picture varied from that of a state of clear consciousness to stupor and coma. Only 2 (those with clear spinal fluids) had a truly clear lucid interval; the others showed some improvement but rapidly lapsed from a confused state into coma.

Aphasia. Six had left sided hematomas. We were able to do modified aphasia studies on 5 of these, and 4 showed an aphasic language difficulty, usually of a mixed type. Of 11 cases with right sided hematomas, only one showed an aphasis and at postmortem examination laceration of the contralateral temporal lobe was found. To what extent the clouding of consciousness contributed to the aphasic picture, of course, is difficult to say, but in each case it was the feeling of the exam-

iners that they were dealing with a specific difficulty in language function.

LABORATORY FINDINGS

White blood count was made in only 10 cases. All showed a polynucleosis and a leucocytosis varying in degree from 9,800 with 76 per cent polymorphonuclears to 17,200 with 86 per cent polymorphonuclears.

In 10 cases *serology of the blood and spinal fluid* was carried out: it was negative in all.

Lumbar puncture revealed the following types of fluid: (a) "Bloody" fluid: 11 of 15 patients had a bloody spinal tap. It should be noted that these cases are too often believed to have clear fluids. (b) Clear fluid: 3 patients had a clear spinal fluid. Two of these cases were diagnosed clinically and the patients were operated on; both recovered. We believe clear fluid indicates good prognosis, and bloody fluid bad. (c) Xanthochromic fluid: this was noted in 1 case on admission, 5 days after injury. The patient recovered. (d) In 2 cases spinal tap was not performed.

Manometric pressure readings varied from 60 to 560 millimeters of water.

The *temperature* varied from 99 degrees F. to 107.8 degrees F. prior to operation. No case with a pre-operative rise of temperature to above 104 degrees F. recovered.

The pre-operative *pulse* rate varied from 32 to 170 per minute. Eight patients showed a drop in the pulse rate to below 60 per minute.

The number and type of *respirations* varied. In no instance was a respiratory rate of less than 16 per minute noted and if the condition was allowed to progress far enough the patients all developed the Cheyne-Stokes type of respiration.

Roentgenograms of the skull were made in 6 cases; in 5, a fracture line crossing the middle meningeal groove or one of the cranial venous sinuses was noted on the side of the lesion and in 1 case a fracture line was demonstrated on the side opposite to the clot. On the whole we believe clinical symptoms rather than roentgenograms should determine the diagnosis.

Four patients had an elevated *blood pressure* prior to operation. One had had hypertension for years prior to the accident. Of the 3 others, 2 died. The patient who recovered had a postoperative drop of the blood pressure to within normal limits. Two patients showed evidences of hypotension on admission to the hospital; both were in shock. We agree with Browder and Myers that an elevated blood pressure is not an accurate index of the presence of cerebral hypertension.

The *mortality rate* is shown in the following table.

MORTALITY RATE

	Case	Lived	Died	Mortality rate per cent
Total number operated on by neurosurgical service	11	5	6	54.5
Total number operated on by general surgical service	4	1	3	75.0
Not operated on (diagnosis not made)	2	0	2	100.0

Postmortem findings. Of the 9 patients who died, 5 were subjected to postmortem examination; all showed an associated skull fracture. Of greater interest, however, is the fact that all these cases had multiple brain lacerations. In 1 there was a contralateral subdural hemorrhage which had been missed because the patient had a trephine opening on one side only, and in 1 an epidural hemorrhage resulting from a laceration of the posterior branch of the middle meningeal artery was missed completely because the trephine opening was placed too far forward. The postmortem findings of the cases which were missed clinically have already been discussed. These findings illustrate the fallacy of speaking of a typical epidural hemorrhage syndrome. In these cases, the clinical picture is usually a result of the combination of brain edema, brain contusion or laceration, *and* the epidural hemorrhage.

SUMMARY

1. Seventeen cases of epidural hemorrhage were seen by members of the Neurological and Neurosurgical Services at the Bellevue

Hospital during the 6 year period from 1930 to 1936.

2. Fifteen of these 17 cases were subjected to operation: the neurological service operated on 11 of these patients with a mortality of 54.5 per cent; the general surgical service operated on 4 of these patients with an operative mortality of 75 per cent.

3. The various signs and symptoms encountered are discussed and an attempt is made to determine various pre-operative prognostic factors.

4. The treatment of epidural hemorrhage has been discussed.

5. The postmortem findings are included and indicate why a "typical epidural hemorrhage syndrome" does not exist.

THE EFFECT OF DRUGS ON DIFFERENT SEGMENTS OF THE INTESTINE OF MAN[1]

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A VARIETY of drugs has been used, clinically, to combat and prevent postoperative intestinal distention associated with adynamic intestinal obstruction or paralytic ileus. Pituitrin and physostigmine, and, in more recent years, peristaltin (Ciba) (a glucoside of cascara sagrada) and acetylcholine have been the drugs which have been considered most effective in overcoming this condition. Our knowledge regarding the ability of these drugs to influence intestinal tone and motility is founded principally on the results of animal experimentation and the impressions acquired by clinical observation of the effects of the administration of these drugs to patients suffering from postoperative intestinal distention. Only a few experimental studies on the intestine of man, as far as we are aware of, have been recorded. These comprise a study carried out by Cross, in which he investigated the effect of pituitary extract and physostigmine on isolated strips of the appendix taken from patients at operation, and a number of studies on humans by other investigators in which the effects of several of these drugs on the gastro-intestinal tract have been observed with the fluoroscope (2, 3, 5, 6). In this paper a review of the literature will not be attempted. This has been done very completely in a paper by Ochsner, Gage, and Cutting, in which the authors reported the results of a similar study carried out on dogs.

On the intestinal service at St. Mary's Hospital, there always are many patients who have had either a sigmoid or a transverse colostomy established for an organic lesion at a point distal in the colon or in the rectum. Occasionally, too, there is the patient who has had an ileostomy performed as the preliminary stage of total colectomy. It was recognized, therefore, that an excellent opportunity was at hand to observe the effects of these drugs on different segments of the human intestine.

THE DRUGS STUDIED AND THE METHOD EMPLOYED IN THE OBSERVATION OF THEIR ACTION ON THE HUMAN INTESTINE

The drugs, whose action on the intestine was studied, were (1) surgical pituitrin, (2) physostigmine salicylate, (3) peristaltin or soluble extract of cascara sagrada, grains 2½ (0.152 gm.) per ampul, prepared for hypodermic injection, and (4) acetylcholine. We observed the effect of these drugs on three different levels of the intestinal tract, the sigmoid flexure, the transverse colon, and the terminal portion of the ileum. In every instance, their administration was by intramuscular injection.

The apparatus employed for recording intestinal movements in the following observations consisted of two pieces of rubber tubing, each of which was ¼ inch in diameter and 3½ feet in length. One end of one of these lengths of rubber tubing terminated in a thin rubber balloon which was 3½ inches in length and approximately the same diameter as the lumen of the intestine. When, therefore, the balloon was inflated to a point short of distention, it filled the lumen of the bowel completely without exerting any tension at the site in which it was lodged. The stoma of the balloon was attached to the end of the rubber tubing by means of rubber cement and tight ligation with linen thread, and in this way the possibility of the leakage of air at this point was prevented. One end of the other length of rubber tubing was connected with a tambour and writing lever. The diaphragm of the tambour, which was composed of the same type of rubber as the balloon, was also fixed in position by means of rubber cement and tight ligation with linen thread, in such a manner

[1]Abridgment of thesis submitted by Dr. John S. Guthrie to the Faculty of the Graduate School of the University of Minnesota in partial fulfillment of the requirements for the degree of Master of Science in Surgery. Work done on Intestinal Service, St. Mary's Hospital, Rochester, Minnesota.

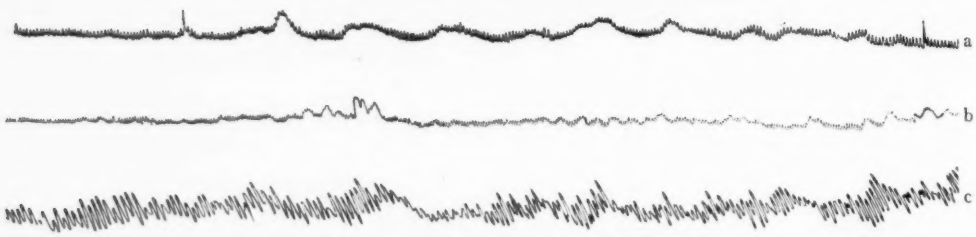

Fig. 1. Kymographic tracing showing the small rhythmic waves of contraction that occur normally; a, in transverse colon; b, in sigmoid flexure; and c, in ileum.

as to insure against the leakage of air from within the recording system at this point. The end of the recording lever of the tambour was fitted with a writing point which would record the intestinal tracings on smooth unsmoked kymographic paper. A single paper kymograph was used and the drum adjusted to rotate at a uniformly slow rate of speed. The free ends of the two lengths of rubber tubing were connected by a three-way stopcock, by means of which air could be introduced into the system and adjusted to the desired degree of pressure. The recording system was carefully tested before each experiment in order to make certain that there was no leakage of air at any of the connections or at any point between the balloon and tambour. During the entire course of this investigation, the physical disposition of the apparatus was not changed.

For each observation we selected patients who had undergone colostomy not more recently than 2 weeks previously, who were in good general condition, and whose bowels and colonic stomas were functioning normally. Care was taken that the patient had not received a laxative or cathartic of any kind for at least 48 hours prior to each observation. During each observation, the patient reclined in the supine position on a couch in a room that had been specially set aside for the carrying out of this study. Hence, the patient, during the entire course of each observation was free of extraneous influences which might cause reflex nervous irritation.

After the recording apparatus had been tested and set in readiness, the rubber balloon was inserted through the colonic stoma and by means of inflation and deflation it was manipulated into its desired position within the lumen of the intestine, at least 2 inches beyond the inner level of the abdominal wall. In order to maintain the balloon in position and to prevent it from being extruded from the intestine by peristaltic activity, the portion of rubber tubing immediately outside the colonic stoma was firmly anchored to the abdominal wall by means of adhesive tape. Air was introduced through the stopcock into the recording system and adjusted to the desired degree of pressure. The writing point was lightly contacted with the kymographic drum, and tracings of intestinal activity recorded.

RESULTS OF OBSERVATIONS

At the commencement of the observations, it was found that when air was introduced into the recording system to inflate the balloon, if the amount that was introduced was sufficient to distend the balloon to a point where it caused tension on the intestinal wall, large strong contractions of the intestine resulted because of the stimulation, mechanical in nature, that was thus produced. These contractions tended to occur every 1½ to 3 minutes and to continue as long as this tension in the balloon was maintained. Because of this, it was necessary to determine the exact degree of pressure essential to render the balloon sufficiently sensitive to record the slightest change in intestinal tone and motility in the kymographic tracing and yet not produce any tension within the intestinal lumen.

It also was observed that the placement of the balloon in the intestine invariably stimulated the bowel immediately to increased peristaltic activity; this did not subside and the bowel did not return to normal until about

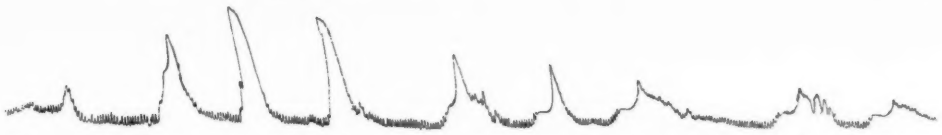

Fig. 2. Kymographic tracing of the transverse colon, showing the huge waves of contraction that occur following the intramuscular injection of 1 cubic centimeter of pituitrin.

half an hour later. Because of this, on each day that observations were made, the tracing always was obtained for at least 1 hour, and care was taken to see that the character of the tracing remained normal for at least half an hour before the drug, to be studied that day, was administered. In this way, the possibility of the drug being credited with having produced an initial excitant effect on the intestine was prevented.

The tracings that are normal for the transverse colon, sigmoid flexure, and ileum are characterized by the presence of a series of small waves that tend to occur rhythmically throughout the length of the tracing (Fig. 1). These waves are not so prominently seen, however, in tracings of the sigmoid flexure. The normal tracing of the sigmoid flexure is represented by more or less of a straight line.

During the entire course of this observation, one drug only, as a rule, was used on the same day and at no time were more than two different drugs used. If two drugs were used, the second was not administered until we were certain that the first drug had not had any effect on the bowel, or until the effect of the first drug had subsided completely. The second drug was not administered until the tracing had continued approximately normal for at least half an hour or more after administration of the first drug.

The transverse colon. In studying the effect of these drugs on the transverse colon, all observations were made on the same patient. This patient was a man who had had a colonic stoma established at the midportion of the transverse colon 6 months previously, for an obstructing lesion of the sigmoid flexure. The balloon was placed in the distal limb of the colon and was therefore free from interference by the fecal current. Observations were made on 9 different days; during this time 1 cubic centimeter of pituitrin was given on five different occasions; 1/100 grain (0.0006 gm.) and 1/35 grain (0.0018 gm.) of physostigmine salicylate were administered on separate days. Four ampuls of peristaltin were administered in 3 days; on one of these days, 2 ampuls were administered, 1 ampul was given 1 hour and 23 minutes after the first. Acetylcholine was given on four different days; the dose used was 100 milligrams the first day, 200 milligrams the second day, and 400 milligrams on the third and fourth days.

Pituitrin. Within 3 to 5 minutes after each administration of pituitrin, huge waves began to appear in the kymographic tracing, which indicated that the drug had caused large powerful contractions to occur in the colon (Fig. 2). These waves occurred every 3 to 5 minutes; the magnitude of each wave gradually diminished until the waves ceased ¾ to 1½ hours later, when the effect of pituitrin on the bowel apparently had subsided. During this time, the patient complained of abdominal cramps, which at first were severe; borborygmus was present and a copious passage of feces occurred from the colonic stoma.

Physostigmine. No apparent effect was observed for ½ to 2 hours following the injection of either 1/100 grain (0.0006 gm.) or 1/35 grain (0.0018 gm.) of this drug. No alteration from the normal occurred in the kymographic tracing. The patient did not experience cramps of even a mild nature; borborygmus was not present, and there was no passage of feces from the colonic stoma.

Peristaltin. On 2 of the 3 days on which 1 ampul of peristaltin was administered, some evidence of action by the drug on the bowel was observed. This was indicated by the appearance in the kymographic tracing of slight to medium sized waves in 3 to 9 minutes after administration of the drug (Fig. 3). These waves continued to occur at irregular intervals of from 1½ to 7 minutes for almost 1 hour.

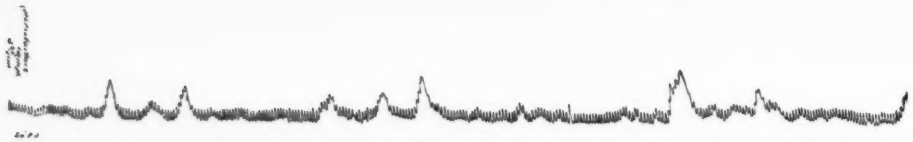

Fig. 3. Kymographic tracing of the transverse colon, showing the irregularly occurring small to medium sized waves of contraction that followed the intramuscular injection of peristaltin.

During this time the patient experienced an occasional mild cramp but borborygmus was not present and the passage of fecal material did not occur from the colonic stoma. On the other day on which this drug was administered, no evidence of its effect was observed in the kymographic tracing, cramps or borborygmus did not occur, and feces was not passed from the colonic stoma.

Acetylcholine. Following the administration of 100 milligrams, 200 milligrams, or 400 milligrams of this drug, no effect on the bowel was observed in the tracing, and there was not any subjective or objective manifestation.

Sigmoid flexure. We observed the action of the sigmoid flexure of four patients, each of whom had had a colonic stoma established in the left inguinal region because of a malignant lesion in the rectum. Observations were made on 7 different days. One cubic centimeter of pituitrin was administered on 4 separate occasions, 1/50 grain (0.0013 gm.) of physostigmine salicylate was administered once, 1 ampul of peristaltin was administered on four different occasions, 350 milligrams of acetylcholine was administered on one day, and 400 milligrams on a second and third day.

Pituitrin. The effect produced by pituitrin on the sigmoid flexure was identical with its effect on the transverse colon. Within 3 to 5 minutes after each injection of the drug, large powerful contractions of the colon occurred; these were evidenced by the appearance in the kymographic tracing of waves of great amplitude. These waves continued to occur every 3 to 5 minutes in gradually diminishing magnitude during the ½ to 1 hour or more that observations were made. Following each injection of pituitrin, the patient experienced abdominal cramps, which at times were quite severe; borborygmus was present and large amounts of feces were expressed from the colonic stoma.

Physostigmine. About 1½ minutes after injection of 1/50 grain (0.0013 gm.) of physostigmine salicylate, small to medium sized waves appeared in the kymographic tracing and these waves continued to occur in the tracing at intervals of from 1 to 8 minutes during the hour that observations were subsequently carried out. The patient, however, did not experience abdominal cramps, even of a mild character; borborygmus was not present, and while there was not any passage of feces from the colonic stoma, gas in somewhat increased amounts was expelled at the times that the largest waves appeared in the tracing.

Peristaltin. On the three occasions on which peristaltin was administered, observations were made for a period of 1 hour or longer after each injection of the drug. On 2 of the 3 days, a few small waves appeared at irregular intervals in the kymographic tracing which indicated that slight peristaltic stimulation of the bowel had been produced by the drug. At no time, however, was there any other evidence of effect on the bowel by the drug.

Acetylcholine. Observations were continued for 1 hour following each injection of this drug. In one instance, about 9 minutes after 400 milligrams had been administered, some increase in the tone of the colon, as indicated by a slight elevation of the base line of the tracing, was observed. This increase in tone was of short duration, however, as the bowel returned to its normal state in about 9 minutes. A few very small waves of contraction also were observed to occur at irregular intervals for about three-fourths of an hour. Aside from this, there was no other evidence of the effect of the drug on the bowel. Cramps, borborygmus, and the passage of feces from the colonic stoma did not occur.

Terminal portion of the ileum and the sigmoid flexure. We observed the effects of these drugs on the terminal portion of the ileum of

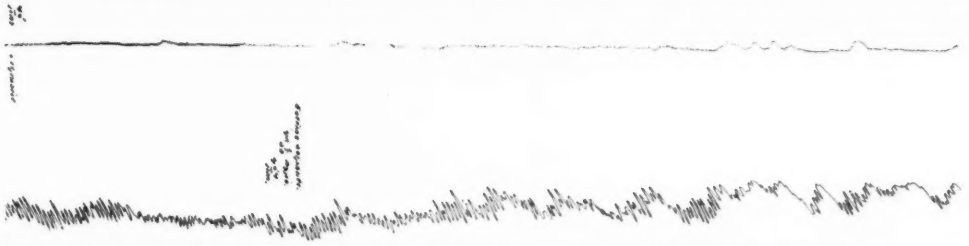

Fig. 4. Synchronous kymographic tracings of the ileum and sigmoid flexure, showing the concurrent effect of the intramuscular injection of 1/50 grain (0.0013 gm.) of physostigmine salicylate on both these segments of bowel. In the ileum, a definite increase in both tone and intestinal movement is seen almost immediately following administration of the drug. In the sigmoid flexure, after a somewhat longer latent period, a slight but definite increase in intestinal movement is apparent.

a man who previously had been subjected to two of the procedures of total colostomy, as carried out in three stages. The first procedure had consisted in the establishment of an ileac stoma; at the second operation a combined abdominoperineal resection of the rectum and the distal third of the sigmoid flexure had been performed. At the time, therefore, that the following observations were made, this patient possessed both an ileac and a colonic stoma. By the employment of two identical recording systems it was possible, by placing the balloon of one system within the lumen of the ileum through the ileac stoma, and by placing the balloon of the second system in the lumen of the upper portion of the sigmoid flexure through the colonic stoma, to obtain synchronous tracings of these two portions of the intestinal tract.

Pituitrin. Within 2 minutes following the injection of 1 cubic centimeter of pituitrin large waves appeared in both the ileac and sigmoid tracings, which indicated that pituitrin had stimulated powerful contractions in both the ileum and the sigmoid flexure. These waves occurred in gradually diminishing intensity every 1½ to 3 minutes during the 55 minutes that observations were subsequently carried out. At the same time, the patient complained of abdominal cramps, at first severe; borborygmus was present and large amounts of liquid feces were passed from the ileac stoma.

Physostigmine. Physostigmine salicylate, grain 1/50 (0.0013 gm.) was administered on 2 different days and observations were made for 1 hour and 40 minutes. Following one of these injections, no effect was evidenced on either the ileum or sigmoid flexure. On the other of these days, almost immediately after the injection of the drug, a definite and prolonged increase in the tone of the ileum was observed, as evidenced by a rather marked elevation of the base line of the ileac tracing from the normal (Fig. 4). Some motor stimulation of the ileum also occurred, as indicated by slight to medium sized waves which appeared every 1½ to 5 minutes in the ileac tracing and continued in gradually diminishing amplitude during 1 hour, 40 minutes that observations were made. With regard to the sigmoid flexure, although no alternation occurred in the tone of this portion of the bowel, slight to moderate sized waves of contraction appeared in the sigmoid tracing about 10 minutes after the administration of the drug, and these continued to occur every 2 to 6 minutes until observations were discontinued. At no time, however, did the patient experience abdominal cramps, and feces was not expelled from the ileac stoma.

Peristaltin. Peristaltin was administered on 2 different days, 1 ampul was the dose administered at each injection. On the first day, 1 ampul only was given, without the production of any apparent effect on either the ileum or colon. On the second day, 1 ampul was given, and this dose was repeated ½ hour later; observations were made for 1¼ hours after administration of the first dose of the drug. Aside from the occurrence of a slight increase in the tone of the ileum, which lasted for about 20 minutes, no other evidence of effect was observed on either the ileum or the sigmoid flexure.

Fig. 5. Kymographic tracing of the ileum, showing the transient increase in tone that occurred following the intramuscular injection of 350 milligrams of acetylcholine.

Acetylcholine. Acetylcholine was administered on 2 different days. On the first day, a dose of 250 milligrams was given, without the production of any apparent effect on either the ileum or the colon. On the second day, following the injection of 350 milligrams, a slight increase in the tonus of the ileum was observed (Fig. 5). This, however, was of short duration; the ileum returned to its original state of tonus about 20 minutes later. Aside from this effect, no other evidence of action by the drug was observed.

At the time of the third stage of the operation all of the colon down to within a short distance of the colonic stoma was removed. This left the patient with a small isolated loop of sigmoid flexure, approximately 3 inches in length, which terminated blindly at its proximal end, and communicated externally by means of the colonic stoma. This small pouch of bowel was known to possess only one small artery. When the patient had recovered sufficiently from the operation, a balloon was introduced into this isolated loop and 1 cubic centimeter of pituitrin was administered to determine if such an isolated loop of bowel would respond to the effects of the drug as did the intact colon. Within a few minutes following injection of pituitrin, contractions occurred in this small segment of colon; these were as powerful and vigorous as were the contractions observed in any of the preceding observations in which this drug was used (Fig. 6).

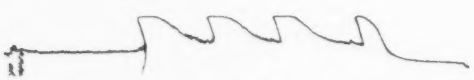

Fig. 6. Kymographic tracing of a small isolated pouch of sigmoid flexure, showing the large waves of contraction that followed the intramuscular injection of 1 cubic centimeter of pituitrin.

SUMMARY AND CONCLUSIONS

A series of observations have been made in an endeavor to determine the effectiveness of surgical pituitrin, physostigmine, peristaltin (Ciba) and acetylcholine as stimulants of tone and motility of the human intestine. Patients who had been subjected to colostomy and ileostomy were observed. By means of a graphic method that involved the introduction of a rubber balloon into the lumen of the transverse colon, sigmoid flexure, and terminal portion of the ileum, it was possible to estimate the effect of these drugs on these different portions of the intestinal tract.

Of these 4 drugs, pituitrin alone was found to be a marked stimulant of the human intestine, and in the light of the results of these observations, it is the only drug of this group that is likely to prove effective regularly as a therapeutic agent in augmenting the peristalsis of an atonic or paralyzed bowel. The effect on the intestine that was observed to follow every administration of pituitrin was so constant that we feel justified in concluding that this drug: (1) is a powerful stimulant of intestinal peristalsis, (2) is consistent and regular in its action, (3) acts with apparently equal strength on both the colon and the ileum, (4) increases the motility of the intestine without apparently exerting any effect on the tonus, and (5) is rapid in its action. Following its administration, it acts within 3 to 5 minutes and its action extends, with gradually diminishing effect, for from ¾ to 1½ hours.

Physostigmine and peristaltin, although they were observed at times to increase the tonus as well as the motility of the colon and the ileum, definitely were found to be inconstant and uncertain in their action. Moreover, the peristaltic contractions which each

of these drugs produced were relatively mild, less regular in their occurrence, and totally lacking in propulsive force as compared with those contractions that followed each injection of pituitrin.

It has been said that, in order to produce the full therapeutic effect of physostigmine on the bowel, a dose of the drug as large as 1/20 or 1/16 grain (0.003 or 0.004 gm.) should be administered. In the instance during this observation, however, in which 1/35 grain (0.0018 gm.) of physostigmine salicylate was administered, the patient shortly after the injection of the drug experienced a feeling of great weakness and dizziness, and marked pallor developed. A similar, though milder, systemic reaction at times followed the administration of 1/50 grain (0.0013 gm.) of the drug. For this reason, larger doses of physostigmine than those employed in this observation were not used.

As regards acetylcholine, the results of this observation would indicate that this drug possesses little worth as a stimulant of the human intestine. On 7 of the 9 occasions on which the drug was employed in doses ranging from 100 to 400 milligrams, no evidence of any effect on the intestine was in any way apparent. On the two occasions on which some increase in either the tone or the peristaltic activity of the colon and the ileum was observed to occur, the stimulative effect of the drug was relatively slight and insignificant, as well as transient in character.

BIBLIOGRAPHY

1. Butler, P. F., and Ritvo, Max. Physostigmine, a peristaltic stimulant. J. Am. M. Ass., 1932, 99: 1329–1332.
2. Cross, D. G. K. The action of physostigmine and pituitrin, alone and combined, upon the isolated human vermiform appendix; the advantages in post-operative ileus. Brit. M. J., 1924, 1: 9–11.
3. Lévy, Max. Etude radiologique de la contraction du gros intestin après injection d'extrait hypophysaire. Arch. d. mal. de l'app. digestif., 1931, 21: 1083–1084.
4. Ochsner, Alton, Gage, I. M., and Cutting, R. A The value of drugs in the relief of ileus. Arch. Surg., 1930, 21: 924–958.
5. Oppenheimer, Albert. Wirkungsmechanismus der Hypophysenhinterlappenextrakte am menschlichen Dickdarm. Deutsch. med. Wchnschr., 1931, 57: 537–538.
6. Pancoast, H. K., and Hopkins, A. H. The action of pituitrin upon the gastro-intestinal tract of man. New York M. J., 1917, 105: 289–292.

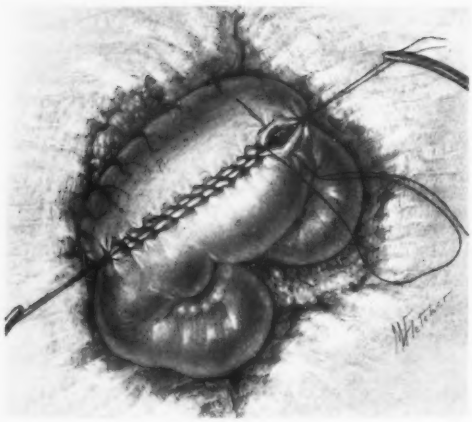

Fig. 1. With the serosal surfaces held in apposition by traction, a continuous suture of silk is placed through serosa, muscularis, and submucosa of the walls of the stomach and the intestine, forming the first posterior suture line of the anastomosis.

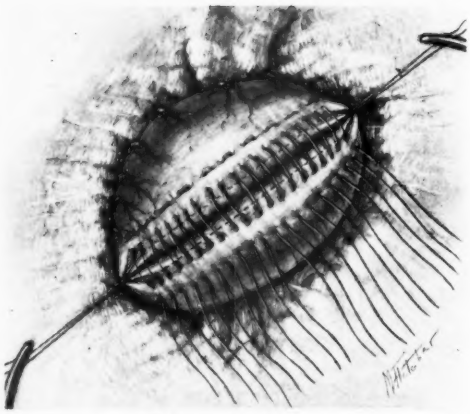

Fig. 2. The mattress sutures are in place five-tenths centimeter apart. These will form the first suture line of the anterior wall of the anastomosis. The dotted lines indicate where the incisions into the stomach and intestine are to be made.

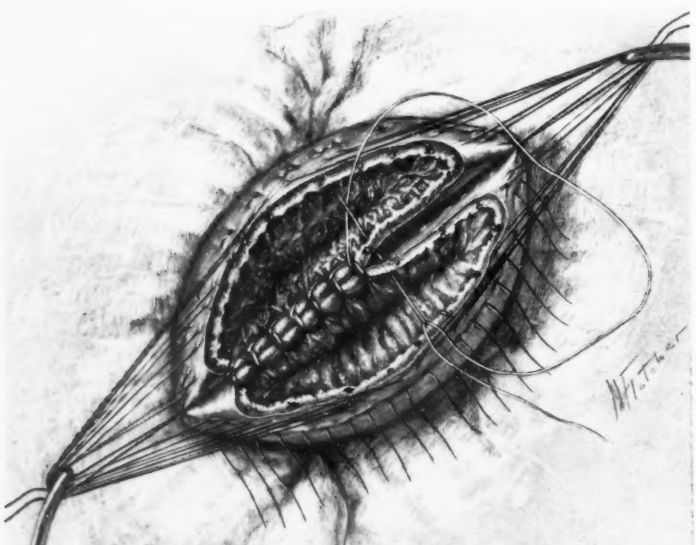

Fig. 3. The mattress sutures have been retracted. The incisions in the stomach and intestine have been made along the dotted lines shown in Figure 2. A continuous lock suture of No. 1 plain catgut is being placed through the wall of the stomach and intestine to form the second suture line and thus complete the posterior wall of the anastomosis. The vessels are shown ligated with No. ∞ plain catgut.

Gastro-Enterostomy.—Frank Glenn.

CLINICAL SURGERY

FROM SURGICAL DEPARTMENT, NEW YORK HOSPITAL

GASTRO-ENTEROSTOMY

A Detailed Description of One Surgical Procedure

FRANK GLENN, M.D., New York, New York

THE medical literature offers many discourses on the comparative merits of the medical and surgical treatment of lesions of the stomach. The controversial points are hotly disputed by physicians, surgeons, and roentgenologists; and different operative procedures are defended by the champions of each. In this profusion of literary material there appear to be few simple and complete descriptions of any one surgical method, excepting the early original papers to re-emphasize the details of one type of gastro-enterostomy, this paper is presented.

Clinical records of patients who died of gastric obstruction may be found in the earliest medical writings. The nature of the obstructing lesion was of little importance in this era, for all patients died of starvation. One of the most dramatic accomplishments of surgery was the relief of gastric obstruction by gastro-enterostomy. This operation was not one of the first procedures to be developed after the introduction of asepsis, hemostasis, and anesthesia; but it has become an accepted and commonplace method of treatment. In general, little thought is given to those who first conceived a surgical procedure, nor to those who subsequently labored to improve it and who brought it to its present state of perfection.

Anton Woelfler, assistant to Professor Billroth, performed the first recorded gastro-enterostomy on a living human being, in 1881. The operation had been devised by his predecessors, Nicoladini in particular, and Woelfler had been instructed by Billroth to attempt the operation when next a suitable case of pyloric obstruction was encountered in the clinic. This moment arrived while Billroth was absent from the clinic; the operation was an anterior gastro-enterostomy for an inoperable carcinoma near the pylorus. It was successful in spite of the fact that the patient was in a deplorable state of emaciation.

Later attempts to perform this operation were less favorable in their outcome. In 1884, Dr. Joseph Ransohoff performed a gastro-enterostomy in Cincinnati. The patient, in a serious condition owing to the presence of a malignant growth at the pyloric end of the stomach, succumbed 8 hours after operation. Ransohoff's was the first attempt to carry out this operative procedure in the United States and, according to him, the seventh to be reported anywhere in the literature.

Various types of gastro-enterostomies have been developed in the 54 years which have elapsed since Woelfler opened up this field of surgery. The early surgeons placed the stoma low on the anterior wall of the stomach; later operators selected a site near the cardia and from there it was shifted to the mid-portion, near the antimesenteric border and finally to the pyloric end

Fig. 4. The mattress sutures have been tied, the reinforcing sutures then placed, and cut as tied to complete the anterior wall of the anastomosis.

Fig. 5. This illustrates a typical stomach with pyloric obstruction. It is dilated to almost three times the size of a normal stomach, although the obstruction was incomplete. Exaggerated peristaltic waves are present.

Fig. 6. The same stomach as shown in Figure 5 after a gastro-enterostomy.

of the stomach. When the posterior gastro-enterostomy was devised by Courvoisier in 1883, with the stoma near the pylorus, the functional results began to improve.

A large variety of sutures have been recommended for use in gastro-enterostomy. Ingenious devices have been manufactured in the hope that an aseptic anastomosis might be secured between the stomach and the intestine. The Murphy button was devised to shorten the operative procedure. Clamps which approximate and hold in position the loop of bowel and the gastric wall and prevent leakage of their contents are in general use today.

Some of the surgeons who have made contributions to the development of gastro-enterostomy are Halsted, Moynihan, Mayo, Walton, Wilkie, and Judd. Gastro-enterostomy is generally conceded to be successful in only 80 per cent of all cases in which it is used. The fact that failures are encountered in 20 per cent of the patients, challenges the surgeon of today to greater effort to improve his technique. It is believed that close adherence to an operative method which has yielded good results may, in part, diminish the unfavorable results in gastro-enterostomy. Such a method is described in full in the following pages. If it does no more than stimulate discussion, this paper seems justified, for where controversy is plentiful, progress may be expected.

PREPARATION FOR OPERATION

Pre-operative preparation of the patient. During his stay in the hospital before operation, the patient is kept in bed and on a liquid diet of high caloric value. Dental hygiene is instituted to diminish the organisms of the mouth which are potential factors in infection.

Pre-operative preparation of the stomach. Many variations in the technique of gastro-enterostomy have been devised to prevent soiling of the peritoneal cavity. It is our opinion that decompression and cleansing of the gastro-intestinal tract before operation is of greater value than any elaborate operative method to obviate contamination of the peritoneum. The stomach which is partially or completely obstructed is usually dilated, its walls are atonic and hypertrophic and bacteria are present in large numbers. Decompression and cleansing of the stomach may be accomplished by gastric lavage once or twice a day over a period of from 5 to 10 days. The result of this treatment is three-fold: (a) the stomach is diminished in size; (b) the gastric walls become more elastic; and (c) the bacterial flora is reduced. Each of the three results of this treatment is of distinct advantage to the operator; there is less danger of infection, the stomach

is easier to handle because it is small, and the anastomosis is more satisfactorily accomplished because the stomach wall is not congested, edematous, and atonic.

OPERATION

The operation was devised by Halsted, who carried out a long series of experiments on lateral and end-to-end anastomoses of the intestine between 1885 and 1890. Later he applied to gastro-enterostomy his findings in lateral intestinal anastomosis and developed the operation which bears his name. The Halsted gastro-enterostomy differs from others in four points: (1) No clamps are used. When clamps are employed in gastro-enterostomy there is danger of injuring the walls of the stomach and intestine. The destruction of some of the gastric wall cannot be considered a serious matter, but loss by devitalization of any intestinal wall is obviously undesirable. The common objection to gastro-enterostomy without clamps is that the contents of stomach and intestine, if allowed to escape into the wound, may cause peritonitis. If the contents of the gastro-intestinal tract have been rendered harmless by lavage before operation, there is little fear of infection. (2) All vessels are ligated individually as they are encountered. It is believed that the clamp, in crushing the wall of the stomach and intestine, temporarily seals vessels which may begin to bleed when the blood pressure is increased, as during postoperative vomiting. When each vessel is ligated separately, there is little danger of hemorrhage after operation. (3) Interrupted sutures are used for part of the closure of the anastomosis. If a continuous suture is placed so that it encircles the entire opening between the stomach and intestine, it tends to contract the lumen and to make its edges rigid. A valve-like action may result which obstructs the passage of gastric contents. By placing interrupted sutures in the anterior section of the gastric wall, this tendency may be counteracted. (4) Silk is employed as suture material to unite the submucous, muscular, and serosal layers of the stomach and intestine. It appears to create less reaction than do sutures of catgut or other material. It is desirable to diminish swelling and congestion around the opening which is made, to insure immediate good function.

Operative approach. The operative approach is through an upper right rectus incision. The opening in the transverse mesocolon should be ample for good exposure of the pyloric portion of the stomach. It cannot always be placed at the desired point owing to variations in the length of the mesentery and in the arrangement of its vessels. When possible it should be to the left of the middle colic artery and parallel to it so as not to disturb the circulation of the mesentery. The upper extremity of the slit should lie at some distance from the large bowel so that the intestinal lumen is not compromised when the mesentery is sutured to the stomach after the anastomosis has been completed.

Choice of site for the anastomosis. When the stomach has been delivered through the slit in the mesentery, it is explored for the purpose of selecting the site for the stoma. To permit early and adequate emptying of the stomach, the artificial orifice should be placed diagonally across the posterior surface of the prepyloric region. At operation this may not be the most dependent portion of the stomach, for the section which appears to be at the lowest point in a dilated stomach, may not retain this position when the organ is reduced in size. An opening placed in the dependent part of a distended stomach may be found, in postoperative roentgenograms, to drain only the upper half of the gastric contents. The stoma should measure about 10 centimeters in length. Traction sutures are placed in the gastric wall so as to mark each end of the contemplated opening, and while they are held under slight tension, a loop of jejunum is brought into the wound.

Two points must be considered in selecting the loop of jejunum to be anastomosed to the stomach. First, the peristaltic waves in it, below the anastomosis, must move in the same direction as the waves in the stomach. Second, the loop of jejunum above the anastomosis must be sufficiently long to prevent tension, but not long enough to permit puddling, or to act as a reservoir for food. The proximal end of the stoma in the jejunum should be 10 to 15 centimeters from Treit's ligament. It should be placed midway between the mesenteric attachment and the opposite free side of the jejunum, i.e., at a distance from the mesentery of about one-fourth of the total circumference of the intestine. The traction sutures, previously placed in the stomach are now carried through the intestinal wall at each end of the site selected for the stoma. Traction on these sutures now brings the serosal surfaces of the stomach and intestine in alinement. In this position a continuous suture of silk is introduced through the serosa, muscularis, and submucosa of each organ so as to form the posterior wall of the anastomosis (Fig. 1). Mattress sutures are now placed so that, if tied, they would unite the walls of the stomach and jejunum at a distance

of about 1 centimeter from the continuous suture line just described (Fig. 2). These stitches are ½ centimeter apart and extend the length of the contemplated stoma. When completed, they are loosened sufficiently to allow an instrument to pass under the slack. A clamp, inserted between the middle mattress sutures and passed under them to one end of the intended stoma, is made to grasp and hold the traction suture while the instrument is withdrawn. The same maneuver is carried out with the traction suture at the opposite end. The site of the stoma may now be exposed by retraction on the traction sutures, which reflect half of the mattress sutures to each side (Fig. 3).

The gastric wall is now incised ½ centimeter from the continuous suture of silk. Bleeding vessels are secured with hemostats and ligated with plain (No. 00) catgut as soon as the stoma is completed. An opening in the jejunal wall in a similar position and of the same length is made. The vessels are caught and tied as in the stomach. Over the initial continuous suture of silk, a continuous lock suture of plain (No. 1) catgut is introduced through the entire wall of intestine and stomach and carried just beyond the extremities of the incisions. When all bleeding from gastric and intestinal surfaces has been controlled, the mattress sutures are tightened. The mucosa is carefully inverted while the walls of the two organs are approximated by drawing up on these sutures. When they are tied, interrupted silk stitches are placed between them to reinforce the closure further (Fig. 4). The transverse mesocolon is now anchored to the gastric portion of the anastomosis with interrupted silk sutures. This prevents herniation of small bowel through the defect in the transverse mesocolon.

The abdomen is closed without drainage. Continuous chromic catgut is used to approximate the peritoneum; stay sutures of a durable, nonabsorbable material, such as silk worm or dermal, are passed through the external rectus sheath down to, but not through the muscle; the fascia is closed with interrupted sutures of chromic (No. 1) catgut; interrupted silk sutures bring the skin edges together.

POSTOPERATIVE TREATMENT

The postoperative treatment begins as soon as the patient returns to bed with the subcutaneous administration of 1500 cubic centimeters of saline solution. Carbon dioxide is given every 2 hours to hyperventilate the lungs. When consciousness is regained, the patient is placed in a low Fowler's position. At this time also, morphine is administered in amounts sufficient to abolish pain on breathing. Patients over 50 years of age may develop pulmonary emboli, and it is felt that shifting the position of such patients every 2 hours, may prevent thrombosis after gastro-enterostomy.

Six to 8 hours after operation 500 cubic centimeters of 10 per cent glucose in saline is given intravenously. If the patient has been depleted by the operation, or if his red blood cell count is low, a small transfusion of blood is preferable. The fluid intake for 24 hours is maintained near a 3000 cubic centimeters total.

The usual regimen after gastro-enterostomy is:

For 48 hours: Nothing by mouth.
Third day: 30 c.cm. of water every hour.
Fourth day: 60 c.cm. of water every hour.
Fifth day: 60 c.cm. of water on the even hour; 60 c.cm. of albumin water or buttermilk on the odd hour.
Sixth day: 90 c.cm. of water on the even hour; 90 c.cm. of albumin water or buttermilk on the odd hour.
Seventh day: 120 c.cm. of water on the even hour; 120 c.cm. of albumin water or buttermilk on the odd hour.
Eighth day: 120 c.cm. of water on the even hour; 120 c.cm. of albumin water or buttermilk on the odd hour. 1 coddled egg morning and evening.
Ninth day: Water *ad lib.* 6 small meals consisting of approximately 45 grams of protein, 120 grams of carbohydrates and 120 grams of fat, and totalling 1,700 calories.
Ninth day to fourteenth: Gradually each feeding is increased from 200 to 500 grams. From the ninth day on, milk, eggs, soup, cereal, bread, meat, vegetables, and fruit are added to the diet.
Fourteenth and following days: 80 grams protein, 220 grams fat, 215 grams carbohydrate. This equals nearly 4,000 calories. It is given in 6 feedings of approximately 500 grams each.

The patient is allowed up on the fourteenth postoperative day; then his fluid and caloric intake are sufficient for his needs. The first fluoroscopic examination is given at this time.

COMPLICATIONS

The immediate postoperative routine described meets the needs of the majority of patients but cannot be adhered to when complications arise. The more common complications after gastro-enterostomy are:

Vomiting. A patient who continues to vomit after the effects of the anesthesia have worn off, sometimes can be relieved by gentle lavage of the stomach with warm saline solution. We believe this procedure to be without danger and it may, by washing out clots or other material retained in the stomach, overcome the tendency to vomit.

Hemorrhage. The best insurance against postoperative hemorrhage is careful ligation of all bleeding vessels during the operation. If there is

evidence of bleeding at any time, a small nasal tube is introduced into the stomach to determine the presence or absence of blood.

Pulmonary complications. These are combated in the usual manner, by change of the patient's position in bed, by hyperventilation of the lungs, and by giving sufficient morphine to abolish pain and allow deep respiratory excursion.

Distention. Distention, especially of the large bowel, should be avoided after gastro-enterostomy. Adequate pre-operative evacuation of the gastro-intestinal tract tends to prevent postoperative distention. In the early stages of this complication the colon may be decompressed by enemas.

Failure of the stoma to function. At the beginning of the second week after operation, when the patient is taking a fair amount of liquid nourishment by mouth, there may develop signs of gastric obstruction which, on lavage, may appear to be almost complete. Under these circumstances the routine diet for the fourth day should be resumed and the stomach lavaged daily. In some instances the obstruction persists through the second postoperative week, after which period the stoma functions perfectly. Postoperative edema and spasm of the small bowel may play a part in the production of such a temporary obstruction. If the stoma proves to be inadequate in size, operative intervention may be necessary.

POSTOPERATIVE X-RAY EXAMINATION

Carty, Weintraub, and Felter have studied large series of patients after gastric operations. They point out that poorly functioning gastro-enterostomies may be earlier determined by x-ray examination than by clinical symptoms. It would appear that there is no better method of estimating the function of a gastro-enterostomy than by its visualization under the fluoroscope after barium has been administered. To determine the result of operation a small amount of barium is given the patient in front of the fluoroscope prior to his discharge from the hospital. No ill effects from this treatment have been noted. The location of the stoma and, to a certain degree, its size may be determined. These are the two variables which account for the majority of poor results after gastro-enterostomy.

The patient is re-examined 6 months after operation. By the end of the sixth month the stoma will have assumed a permanent position and size. Fluoroscopic examinations are, thereafter, limited to 1 a year, if the patient is free of complaints referable to the gastro-intestinal tract. Beginning marginal ulcers and recurrent ulcers may be discovered by x-ray before marked symptoms have appeared, and treatment can be instituted at once with the avoidance of serious late manifestations and complications. The treatment may consist in enforced rest and careful adherence to a rigid diet. However, it may demand surgical intervention. If this is the case, then surgery may be undertaken before perforation occurs; an incident which obviously adds to the risk of operation. If the surgeon is present and makes the observations with the roentgenologists, he has an opportunity to study his cases with a view of improving his operative procedure.

The 2 roentgenograms illustrate the value of this form of check on the results obtained.

Figure 5 illustrates a typical stomach with pyloric obstruction. It is dilated to almost three times the size of the normal stomach, although the obstruction is incomplete. In Figure 6, the same stomach is shown after gastro-enterostomy. All the requirements for a good therapeutic result are present; the stomach has markedly decreased in size, the stoma is near the pylorus and, although the exact diameter is not visualized, it is adequate, for only a small amount of barium is retained in the stomach; the duodenum and jejunum may be seen from the pyloric sphincter to the anastomosis; the loop is not sufficiently long to permit puddling. The distal loop functions well for the barium has penetrated into the small intestine below the anastomosis.

BIBLIOGRAPHY

1. Billroth, T. Report on Billroth's operation. Wien. med. Wchnschr., 1881, 595: 634.
2. Carty, J. R., Weintraub, S., and Felter, R. K. An x-ray study of the post-operative stomach. Radiology, 1934, 22: 191.
3. Courvoisier, L. Zentralbl. f. Chir., 1883, 10: 794.
4. Halsted, W. S. Surgical Papers. 1924, 1: 181.
5. Judd, E. S. Ulcer of the stomach and duodenum. Minnesota M. J., 1926, 6: 311.
6. Judd, E. S., and Rankin, F. W. Technique for resection of gastric and duodenal ulcers. Surg., Gynec. & Obst., 1923, 37: 216.
7. Mayo, W. J. Review of 500 cases of gastro-enterostomy. Ann. Surg., 1905, 42: 641.
8. Moynihan, B. Abdominal Operations. Vol. 1, p. 244.
9. Murphy, J. B. Cholecysto-entero-anastomosis. Med. Rec., 1892, 42: 665.
10. Nicoladini, C. Quoted by Anton Woelfler.
11. Ransohoff, J. Case report. Med. News, 1884, 45: 578.
12. Walton, A. J. Gastrojejunal ulceration. Brit. J. Surg., 1934, 22: 33.
13. Wilkie, D. P. D. Gastric surgery. Edinburgh M. J., 1919, 23: 319.
14. Woelfler, Anton. Gastro-enterostomie. Zentralbl. f. Chir., 1881, 45: 705.

CARE OF THE RUPTURED APPENDIX[1]

Reduction of Mortality to Four Per Cent in Series of Fifty Cases

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APPENDICITIS is a disease of common occurrence and of great diversity in its clinical course. It is so often of extreme gravity, especially in young subjects, and so disconcerting in its evolution, that its treatment may be said to be always a matter of deep solicitude to the surgeon. He must be prepared to grapple with it at a moment's notice, as it were, and muster all his skill and knowledge to win the fight.

So real, however, has been the progress within recent years in its surgical treatment that, aside from accidents and complications such as embolism, ileus, and other obstructive or inflammatory sequels, the unruptured appendix should carry little or no mortality. This is true whether the organ be chronically inflamed, of interval type, or in a state of acute inflammation. It is for this reason that physicians and even well informed lay persons insist upon immediate operation as soon as the diagnosis of appendicitis is made.

At the outset, the diagnosis may not be one of absolute certainty, nevertheless no time is to be lost. It should be remembered that the conditions which present similar symptoms are likely to be those of equal urgency, such as obstructions of the bowel, intussusception, volvulus and the like, so that the surgeon is fully justified in opening the abdomen immediately to find the source of the trouble.

HIGH MORTALITY IN APPENDICITIS

Notwithstanding the real progress that has been made in the surgery of acute appendicitis, and paradoxical as it may seem, the figures of the United States census show a gradual but steady rise in the mortality from appendicitis since this century came in. This increase has been from 9.7 per 100,000 of population in 1900 to 15.2 per 100,000 in 1932. The figures given by Fitz for Massachusetts are very similar: a death rate of 8.7 per 100,000 in 1900 had become 14.4 per 100,000 in 1933. In 1900 only 243 cases in that state terminated fatally, but in 1932 the number was 623.

In interpreting these figures, we must, of course, bear in mind the fact that in 1900 the diagnosis of appendicitis was not so frequently or so properly made as is the case today. Many a death certificate was undoubtedly labeled "acute indigestion," when the true cause of death was appendicitis. Yet the fact remains that the mortality from appendicitis is alarmingly high in view of our knowledge of the proper treatment of this disease.

It is the gangrenous, or the gangrenous and ruptured, appendix that accounts for this high mortality of appendicitis generally. For it appears that, while the unruptured appendix has frankly yielded to modern scientific surgery when this is available, an increasing number of afflicted appendices either receive no early treatment at all or are coaxed along by antiquated methods until the suffering organ has perforated. These cases account for the high mortality in appendicitis.

Reviewing 3,913 operative cases of appendicitis, Finney in 1933, reported that in the 5 year period 1926–1930, inclusive, 18.17 per cent of the appendices concerned had ruptured before they came to operation—a statement that surely does not entitle us to feel much complacency. In his general peritonitis group of 240 cases, there were 54 deaths, a mortality of 22.08 per cent, with danger multiplied by about 5 times over the abscess group (with 4.57 per cent mortality), and 225 times over the group of cases treated in an early stage. These figures were from a large group of cases cared for by family physicians and representing the average mortality.

In a study based on 220 cases, Coudert, in 1929, observed 7 deaths in the group of 20 patients with general peritonitis, which thus represented a 35 per cent mortality in this class. Of Black's 14 fatal cases of acute appendicitis with local or general peritonitis, no fewer than 7 (50 per cent) had suffered a ruptured appendix. Haggard had a mortality of 24.7 per cent from gangrene, and Wilkie states that 90 per cent of deaths in appendicitis are in cases not of primary inflammation but of primary obstruction with resultant tension, gangrene, and perforation.

As Labbé points out, it is impossible during the first 12 hours to distinguish between those cases that will run a benign course and those that are destined to assume a graver form; hence it is imperative to operate immediately upon making the diagnosis of acute appendicitis. Carried out at this time, the operation is a simple and benign

[1] From the Department of Surgery, DeCourcy Clinic.

procedure, a precautionary measure designed to forestall an uncertain and unpredictable future. It is foolhardy to wait for more disturbing symptoms to force the surgeon's hand.

HOW TO LOWER MORTALITY

I feel that two avenues to lower this alarming mortality are open to us: (1) the continuous and increasingly vigorous education of the public to the dangers of procrastination; (2) improved technical handling of the ruptured cases so as to save many of the patients who are now being lost.

With reference to the first of these needs, we all know that many patients with appendicitis resort to self-medication in the early stages of the attack, thus losing valuable time before the advice of a physician is sought. It is so easy to ask a druggist for something that will relieve a pain in the abdomen and to be given a sedative or more probably a cathartic.

The use of cathartics is especially objectionable. It was reported by Heyd that of 902 patients with acute appendicitis who took a cathartic, 1 in 14 died; of 992 who took two or more purges, 1 in 7 died; whereas of 402 who took no laxative, only 1 in 80 died. In Kehl and Rentschler's series of 126 cases, all but 2 of the 16 who died had been given cathartics, usually castor oil, before admission to hospital.

Too often the patient supposes that the pain in appendicitis must always be low down on the right side and so discards the thought of appendicitis because his pain is localized somewhere else. He does not know that delay may mean peritonitis and death. In some cases of insidious onset he may not even notice the earlier symptoms, may not be aware of anything more than a vague discomfort in the intestinal region and slight bowel disturbance, and thus fail to seek aid until the appendix has actually burst and peritonitis has arrived. Such cases are, to be sure, atypical. In cases in which the attack begins with acute pain, the patient is driven to the physician by his suffering. It is strongly incumbent upon the latter to impress the patient with the urgent necessity of hospitalization and early operation to avoid the complications that are almost inevitable with delay and the danger of possible death if a procrastinating course is pursued. Delay before operation must be recognized as the chief factor in the death of these patients.

But it is in the second of these avenues of approach to a lowered mortality that this paper is especially interested. Wherever improvements in operative technique and in the pre-operative and postoperative handling of the ruptured and gangrenous appendix have been adopted, they are already bearing fruit in a lessened death rate.

TABLE I.—MORTALITY FROM APPENDICITIS AT GOOD SAMARITAN HOSPITAL (1931–1935)

	Cases	Deaths	Mortality percentage
1931			
Acute	358	11	3.1
Subacute	113	3	2.7
Chronic	201	2	1.0
Perforated	64	11	17.1
Total	736	27	3.7
1932			
Acute	304	14	4.6
Subacute	116	0	0.0
Chronic	191	1	0.5
Perforated	55	10	18.2
Total	666	25	3.7
1933			
Acute	340	11	3.2
Subacute	112	1	0.9
Chronic	162	0	0.0
Perforated	49	12	24.5
Total	663	24	3.6
1934			
Acute	379	16	4.2
Subacute	158	4	2.5
Chronic	152	0	0.0
Perforated	39	9	23.1
Total	728	29	3.9
1935			
Acute	400	16	4.0
Subacute	177	0	0.0
Chronic	145	0	0.0
Perforated	35	4	11.4
Total	757	20	2.6
Total number	3550	125	3.5

With a view to showing the results that have been achieved by applying these newer operative methods at the Good Samaritan Hospital in Cincinnati, I have prepared the accompanying table, based on 3,550 cases of appendicitis taken from the files of that hospital and covering the 5 year period 1931–1935, inclusive. Table I records the number of cases of acute, subacute, chronic, and perforated appendicitis, together with the number of deaths in each category and the percentage it represents for each year and for the entire 5 year period. The incidental appendectomies done while operating for other conditions are not included.

It will be seen that the subacute and chronic cases carry a mortality of about 1 per cent. Wherever the appendix ruptured, the total mortality rose to between 11.4 per cent and 24.5 per cent, averaging about 18.9 per cent over the 5 year period, but with 11.4 per cent for its latest and lowest mortality figure for any single year, that of 1935. Under the chronic cases are included the interval appendectomies.

In my last series of 50 cases of perforated appendix in which the cecum has been decompressed at the time of operation, the mortality for such cases has been only 4 per cent—a reduction of 13 per cent. Furthermore, both deaths in the series were in cases in which patients had generalized peritonitis at the time of operation.

DECOMPRESSION OF CECUM

During the past 2 years we have made a number of modifications in the technique of appendectomy. Following removal of the ruptured appendix, I have, in a large number of cases, inserted a Pezzer catheter into the cecum, and recently I have been inserting it in practically every case of ruptured appendix. The catheter is introduced through the cecal opening after removal of the appendix, and two fine linen purse-string sutures are applied. A soft rubber drainage tube is carried into the cul-de-sac and another one is inserted into the iliac fossa to prevent secondary abscesses. These two drainage tubes are removed on the tenth day after operation. A clamp is placed on the distal end of the catheter in the cecum. This is removed from time to time to permit escape of gas or possible fecal material.

The main purpose of this cecal catheter is to permit decompression of the bowel before distention occurs with resulting paralysis. Wilkie has pointed out that there are two primary and fundamental processes which occur in appendicitis: one is the acute infection of the wall of the appendix; the other, an acute obstruction of the lumen of the appendix, comparable to any other type of obstruction of the bowel. In the former, the rise of temperature is natural and inevitable. But in the obstructive type, this rise is absent during the early phase, at the very time when diagnosis is all important.

While Wilkie does not agree that obstruction precedes infection in all cases, he does believe that blocking of the lumen, with consequent tension, is the real danger in appendicitis. In cases in which this factor is pronounced, a cecostomy or enterostomy is indicated, such as would be appropriate in any other type of intestinal occlusion. The distention hinders the circulation in the wall of the appendix, which then loses its power of resistance. Relief of this tension by a cecostomy will accordingly render a service to the inflamed peritoneum by improving the blood supply.

This cecostomy opening, however, serves not only as an adequate valve for the escape of gas but also as an inlet for fluid to counteract dehydration. The Murphy drip is given at regular intervals through the inserted catheter. It has the advantage of bringing fluid to just that part of the bowel where it can be best absorbed. This is far from true of the drip given by rectum, where retention of fluid may be quite difficult in view of the natural excretory function of that organ. In the case of young children the cecum is a particularly practical point for giving the drip, avoiding wetting or soiling of the bed. The cecal fistula can also be used for the administration of enemas and for flushing out the bowel at intervals as may be required.

In the past, many a surgeon has observed that the appearance of a spontaneous fecal fistula during the course of an appendicular peritonitis has resulted in almost immediate cessation of alarming symptoms and in marked improvement in the patient's general condition. A cecostomy drainage deliberately placed has the same therapeutic effect, and in addition has a tendency when no longer needed, to close spontaneously, which is quite different from the behavior observed in an ordinary persistent fecal fistula. The catheter usually starts to drain within 24 hours, and drainage continues for 4 or 5 days. After this the drainage from the catheter lessens and the bowels move naturally. The stay in the hospital in cases in which the cecum has been drained and in which no complications have arisen has averaged only 3 weeks, and the fistula closes completely within a month. This outcome is unlike that of the spontaneous fistula, which usually takes 6 to 8 weeks to close.

We do not claim that every patient with general peritonitis will recover through use of the method of decompression; but we do assert that it is becoming the usual thing to see patients recover who formerly would have died, and the convalescence under these conditions is not nearly so stormy as it was under old methods. Dorrance and Nealon report that they have used this method with excellent results in 30 cases, securing effective decompression of the intestine by providing an outlet for gas and fecal material.

The question may be raised whether it is necessary to drain the bowel in every case of ruptured appendix. The answer is, probably, that it is not; but until we know on which ones to do an enterostomy and on which ones not to do so, it is safer to employ the method in all. Formerly nature came to the rescue of these patients with a fecal fistula to relieve distention, but she did so rather late; or we did a secondary enterostomy, also late, when distention and frequently paralysis had already occurred, and then it was too late.

In some of our cases we use continuous gastric lavage to supplement the cecal catheter in high obstruction or high ileus, where vomiting is persistent and the patient accordingly suffering with dehydration and loss of secretions from liver and pancreas; but this is not needed nearly so frequently as the cecal fistula. In order to rehydrate a patient who has lost essential fluids by vomiting, either gastric or duodenal lavage is instituted through the nasal catheter by the continuous method, as advised by Wangensteen. Intravenous or subcutaneous injections of glucose and chlorides are given routinely, and the Murphy drip is carried out through the cecostomy wound. In short, any method that will succeed in accomplishing the replacement of lost fluid is pressed into use, and it is astonishing to see how rapidly the prostrated and collapsing patient is restored to relative comfort by this restoration of fluid equilibrium.

INCISION AND DRAINAGE

As regards the type of incision for reaching the appendix, it seems to me that this is not so important as some surgeons would have us believe. There is very little difference between the point of entrance of the Kammerer, or outer right rectus incision, and the McBurney. The fact is that the McBurney incision extends to the margin of the right rectus and frequently overlaps the muscle. It exposes more raw surface to infection and does not permit cul-de-sac drainage as readily as the lower right rectus incision. This, in my opinion, is a disadvantage, especially when diffuse pelvic peritonitis is present. Secondary cul-de-sac abscesses are more frequent than is generally supposed.

We all agree, I think, that if a localized abscess is present, the incision should be so placed as to provide the best facilities for drainage. With the patient in the usual Fowler position after being put back to bed, the pus drains ideally by this method. We are absolutely opposed, with McGrath and Eiss, to the unsound practice of simply draining in the presence of localized pus and leaving the appendix alone. Some surgeons do this because they are afraid of spreading an infection that shows signs of walling off, or because owing to adhesions they cannot find the appendix. We feel strongly, however, that an operation for appendicitis that does not remove the appendix is only a palliative measure and invariably invites sequels, paving the way for stronger adhesions and more inflammatory and fibrous changes that will ultimately require renewed surgical measures of a more radical nature. With proper caution, through a wide incision, the intestines can be packed off completely with moist pads; the plastic adhesions, usually not yet tough, can be carefully loosened; the pus can be aspirated; the appendix can be found and removed; and the cavity can then be thoroughly cleaned out and closed, with or without drainage according to the individual case.

RELIEF OF DISTENTION

We are convinced that the peritoneum can take care of extensive infection even in presence of general peritonitis, *provided the bowel does not become distended*. It is distention that we have to fear more than infection, for distention impairs circulation in the gut walls and leads more quickly than anything else to gangrene. We find Wilkie insisting that blocking of the lumen with tension is the real danger in appendicular disease and advocating cecostomy or enterostomy according as the large or the small bowel is more affected. Such relief of intra-intestinal tension will, among other things, render a service to the inflamed peritoneum by permitting a more efficient blood supply.

With the source of infection removed, the peritoneal cavity is generally capable of taking care of itself, say Willis and Mora. Consequently, with the ruptured and gangrenous appendix out, they regard drainage of the cavity as unnecessary. They believe that it does not subtract from the mortality but, on the contrary, adds to the morbidity. A study of 100 cases convinced them of the comparative safety of closing the abdomen without drainage in acute suppurative appendicitis.

Haggard has seen gangrene present as early as 6 hours after the first symptoms of appendicitis and states that it usually develops within 24 hours, again supporting the view that it is obstruction of the lumen of the appendix that causes the fulminating cases in which the patient is gravely ill from the start with agonizing and continuous pain and persistent vomiting. This indicates what is to all intents and purposes an intestinal obstruction, ending in death of the appendix with almost certain gangrene and perforation unless promptly operated on. But when the distention is relieved, the peritoneum has strong resources within its own circulating blood for combating the infection.

When the peritoneal cavity is found full of free pus, this should be carefully aspirated, never irrigated as was done of old. Irrigation only serves to disseminate the infectious material. Modern surgery has renounced this method and concen-

trates on a search for the offending appendix, after removal of which the surgeon, more at his leisure, may seek out and drain any secondary or aberrant collections of pus, which may sometimes be at a distance, as for example in Douglas' cul-de-sac, under the liver, or in the left iliac fossa.

Apparently the difference in the amount of distention is the reason for the differences observed in the rapidity with which appendicitis brings on a diffuse peritonitis. Twenty-four hours in one patient will do as much mischief as 3 days in another. Some patients have a generalized infection in a single day, while others within the span of a week have little more than a lymphatic exudate around the appendix. Too many unknown factors exist, however, to make it permissible to postpone operating under any circumstances.

Let me emphasize again that loss of time when the patient is in a state of distention is the chief cause of the mortality from ruptured appendix. To save time must be the primary consideration. The patient is absorbing toxins; the circulation of the gut is obstructed; death is imminent.

When a patient presents symptoms of appendicitis, no matter how mild, the only safe course to pursue is that of immediate hospitalization and prompt operation for the removal of the appendix. Delay leads fatally to those dangerous complications with gangrenous and finally ruptured appendix, with distention from obstruction of the lumen and impairment of local circulation, all too frequently terminating fatally within the span of a few days or even a few hours. No surgeon can ever know at the outset whether the case presenting itself is going to be one of these fulminating cases. I am accordingly convinced that prompt removal of the appendix and relief of distention by cecostomy are the only means by which the surgeon can do justice to his patient. The results in reduced mortality after use of the method bear eloquent testimony to the validity of this point in view.

CONCLUSIONS

1. It is the gangrenous or the gangrenous and ruptured appendix that accounts for the high mortality of appendicitis.

2. Improved operative technique in handling ruptured appendices will save the lives of many patients.

3. Death in cases of ruptured appendix is due more to distention from intestinal obstruction than to infection of the peritoneal cavity.

4. The peritoneum can successfully withstand extensive infection even in cases of general peritonitis, provided the bowel does not remain distended.

5. Relief of distention by placing a decompressive cecostomy following appendectomy is indicated in all cases of ruptured appendix.

6. Results of decompressive treatment warrant the belief that a greatly lowered mortality rate will follow the increased application of the method.

REFERENCES

1. Black, J. M. Survey of 340 cases of acute appendicitis. Brit. M. J., 1932, 2: 1136.
2. Coudert, E. L. Quand et comment convient-il d'opérér l'appendicite aiguë. Thèse de Paris, Paris. Librairie Louis Arnette, 1929.
3. Dorrance, G. M., and Nealon, S. W., Jr. Use of cecal drainage in ruptured appendicitis. New York State J. Med., 1935, 35: 119.
4. Finney, J. M. T., Jr. Appendicitis; some observations based on review of 3913 operative cases. Surg., Gynec. & Obst., 1933, 56: 360.
5. Fitz, R. On perforating inflammation of vermiform appendix with special reference to its early diagnosis and treatment. New England J. Med., 1935, 213: 245.
6. Haggard, W. D. Appendicitis; analysis of 3344 cases with remarks on delayed operation in delayed appendicitis. Am. J. Surg., 1935, 28: 71.
7. Heyd, C. G. Death from appendicitis; preventable mortality. Am. J. Surg., 1934, 26: 317.
8. Kehl, G. W., and Rentschler, C. B. Acute appendicitis complicated by peritonitis; immediate and late results in 126 consecutive cases. Am. J. Surg., 1935, 29: 373.
9. Labbé, E. L. Contribution a l'étude du traitement de l'appendicite aiguë. Thèse de Bordeaux, 1929.
10. McGrath, J. J., and Eiss, S. Prevention of late postoperative complications in acute suppurative appendicitis, with 3 case reports. Am. J. Surg., 1935, 27: 112.
11. Wangensteen, O. H. Practical aspects of therapeutic problems in intestinal obstruction. Internat. Clin., 1935, 3: 227.
12. Wilkie, D. P. D. Some principles in abdominal surgery. Surg., Gynec. & Obst., 1930, 50: 129.
13. Willis, D. A., and Mora, J. M. Relation of drainage to morbidity following operation for acute suppurative appendicitis. Am. J. Surg., 1935, 27: 480.

TREATMENT OF FRACTURES

Further Observations on the Use of Splenic Extract

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THE idea of a splenic extract diet was suggested by the work of Otto Fliegel who fed raw spleen to patients with bone and joint tuberculosis. The present paper is the outcome of this idea and its development, for the question very soon arose whether, if splenic extract treatment can be used in tuberculosis of the bones and joints, why not in fractures (new and ununited), in osteomyelitis, and in rachitis?

In 1933, the writer[1] described the use of splenic extract in the treatment of bone and joint tuberculosis, over a period of 2 years. The results were summarized as follows:

1. The use of splenic extract in the diet of patients suffering with bone and joint tuberculosis has been found very beneficial, as improvement is noted in the febrile condition, the local reactions, the growth, the weight, the color, the appetite, the blood composition, the deformity, the complications, the roentgen picture, the activity permissible to the patients and the dispensing with support.
2. Improvement from splenic extract treatment probably will be more apparent to those who are unable to enforce a strict compliance with the accepted ideal treatment, i.e., support, recumbency, heliotherapy, proper feeding and proper aeration.
3. The production of splenic extract is possible and the distribution is practicable.
4. It is possible to obtain the co-operation of patients in adopting the splenic extract diet, even of those in remote sections.
5. Splenic extract treatment has also produced improvement in osteomyelitis (acute and chronic) and in ununited fractures. This investigation is well under way.
6. Enough improvement has been shown in the blood composition to stimulate further study of this phase.
7. The writer cannot explain the improvement gained by the administration of splenic extract. Various explanations given so far may all be true, but these investigations lead to the belief that as yet there is no certainty as to which is the most important factor.

While the report of Barr does not confirm this, he has been good enough to leave the matter open. The writer explains Barr's opinion first upon the basis that Barr carried out the splenic extract diet only for 6 months, which is not a sufficiently long time, and second, upon the fact that Barr's patients were already receiving such superb treatment (Peabody Home, Boston, Massachusetts) that the small degree of improvement possible was hard to ascertain, while the writer's cases were collected from a group in which the excellent treatment of Barr was impossible. Hence, the improvement gained by him by splenic extract diet was very evident.

The late Dr. Eikenbary through his associate, Dr. John F. LeCocq and assistant, Dr. J. N. Nelson, duplicated the work of Barr and of the writer, and their results would appear to confirm those reported by the writer.

In 1933, I was unable to explain definitely why these cases of bone and joint tuberculosis improved under the treatment with splenic extract but at the same time I had noted improvement in acute and chronic osteomyelitis and in ununited fractures. As there is calcium deposition in the healing of bone and joint tuberculosis, and as this is also the case with acute and chronic osteomyelitis and ununited fractures, the work of ununited fractures was pushed along as a definite investigation, with the idea in mind of the probability of being able to work out a solution of the physiological action of the splenic extract. And from this investigation the writer now feels that he can make some deductions.

The present paper is designed to show the effect of splenic extract diet upon the healing of fractures. Among the 45 cases which he is reporting here, there have been 3 failures, and all three of these failures fall in the series of cases in which bone grafts were performed. Two of these were fractures of the femur, with massive grafts, and 1 was a fracture of the humerus with a massive graft. In 1 case it is impossible to explain the nonunion of the fractured femur on any grounds. The case of fracture of the humerus had been operated upon originally by some one else and was understood to have had an infection of the previous graft. One case of fracture of the femur, operated upon by the writer, with a massive graft, had an infection as a result of an old compounding of the fracture which had been healed for a year and was therefore considered by the writer to be quiescent at the time of the operation. It is interesting to note, however, that in spite of the fact that union did not take place completely, the graft did unite so solidly to the proximal end of the distal fragment that at the time of a second operation, the graft had grown so firmly into the proximal end of the distal fragment that the cleavage line could not be found, and it was impossible to remove the original graft. The graft was therefore cut off

[1] J. Bone & Joint Surg., 1933, April.

evenly with the proximal end of the distal fragment and the distal portion of the graft was left completely ingrown into the proximal end of the distal fragment. This would lead one to believe that the splenic extract diet had helped to a great extent, and that another factor, probably the infection, was wholly to blame for the persistent non-union.

The problem was attacked very cautiously, and splenic extract was used at first only as an adjuvant. In other words, it was used only to supplement the other procedures in the treatment of ununited fractures. The first series of cases consisted of those in which bone graft operations were performed. In this series of cases—8 in number—it was found that not only did union occur more quickly and more firmly than would ordinarily have been expected, but the condition of the bone as a whole was improved. In Case F.1., S.V.-2, the cortex of the bone at the time of the operation was found to be of only egg-shell thickness. It could be cut with an osteotome almost by pressure of the hand alone, without a mallet. Not only did union take place, but in 60 days the degree of union was unusual, and in 98 days (14 weeks) union was perfectly solid. In Case F.2, S.V.-2, because of the result already experienced in several cases, it was decided to abandon the massive type of graft and to use only a small graft, to hold the ends of the fragments of the femur in apposition. Due to poor facilities, even the position was not perfect, but in spite of this a mass of calcium was deposited so great that the writer was thrown into consternation. The conclusion that splenic extract induced an unusual deposit of calcium now seemed unavoidable.

The second series of cases—12 in number—was begun then. Fortunately, at this time the writer had a considerable number of fractures in which the position of the fragments was good, although lack of union had persisted from 7 to 12 months. This group consisted of cases that were treated by the administration of splenic extract and the use of crutches alone. No other treatment was instituted, as in these cases other procedures had been exhausted. The serial roentgen-ray films of Cases F.3, S.V.-2, F.4, S.V.-2, F.5, S.V.-2, and F.6, S.V.-2 speak for themselves.

These observations seemed to encourage the writer's inference that the administration of splenic extract did stimulate the deposition of calcium. A third series was then started. This series consisted of 10 cases, which had been referred to the writer, of fractures united more or less in bad position after a duration of time (3 to 4 months). Following the proper reduction of these fractures, the patients received splenic extract. While it is true that following the proper reduction of fractures which have been in malposition for some time, in which there is little union, healing is expected with this procedure of reduction alone, Case F.7, S.V.-2 illustrates the writer's point that the deposition of calcium following reduction in those patients treated with splenic extract diet is more advanced than in those patients without the diet, and by comparing the rapidity of the calcium deposition between the time of the fracture and the reduction (8 weeks, during which no splenic extract was administered) and the deposition between the reduction and the time the postoperative film was taken (4 weeks, during which time the patients received splenic extract), the comparable increase can be noted.

The fourth series consisted of 1 case, that of a white girl, 14 years of age, with fragilitas ossium. This patient had received every known treatment by leading men throughout the world, without avail, and in addition osteotomies, performed for correction of deformities in the past, had not healed when she was brought to the writer, in spite of the fact that the osteotomies had been performed some years previously. Upon the splenic extract treatment, not only did the general condition of the bones as a whole markedly improve, but the non-union present definitely became solid clinically and also improved roentgenologically. This case is especially important in that the calcium and phosphorus balance showed a retention of calcium before treatment of 0.235 and a retention of phosphorus before treatment of 0.259, and following treatment with splenic extract over a period of six months showed a calcium retention of 0.770 and a phosphorus retention of 0.945. The calcium phosphorus balance had been run in other cases (Table I) of the 45 which comprised the total group, but this is the only illustrative case in which the calcium phosphorus balance was run, and it seems to confirm the writer's findings, that calcium deposition is stimulated by the splenic extract. When this patient was first seen by the writer she could hardly walk, at best waddling with assistance, using two special canes. At the present time she rides horse back and is entirely independent. The canes are being continued as a protective agent only.

The fifth series of cases was that in which fresh fracture cases were treated with splenic extract. There were 14 of these cases. Case F.9, S.V.-2 indicates the unusual activity of union.

It was now felt that it had been proved clinically that splenic extract does forward the healing of fractures. The problem of animal experi-

mentation was next approached. Four dogs of the same sex, breed, size, and weight were chosen. These dogs were from separate litters. One femur each of two dogs was osteotomized, and 1 tibia each of 2 other dogs was osteotomized, by open operation. The wounds healed in each case by first intention. No splints were applied. One of the 2 dogs whose femora were osteotomized and one of the 2 other dogs whose tibiæ were osteotomized were put upon the splenic extract. The 2 other dogs were fed a regular diet without spleen. Clinically the union of the fractures in the dogs upon the splenic extract diet was very much more rapid and firm than the union in the dogs which were not fed splenic extract. At the end of 69 days (9 weeks), all dogs were killed and a block of tissue taken through the fracture line of each of the specimens. The histological report of the pathologist is quoted as follows: "These specimens, all blocks of similar size, were placed in decalcifying solution (strong formaldehyde 10 c.cm.; distilled water 90 c.cm.; nitric acid 20 c.cm.). From time to time I tried specimen No. 1 to determine the degree of decalcification. When decalcification was complete in No. 1, the tissues were all washed free of acid and again placed in 10% formaldehyde. Much to my surprise and chagrin I found, when I started to make the sections, that specimens 1 and 3 were properly decalcified while specimens 2 and 4 were so digested by the acid that good sections could not be made. Specimen No. 1: The periosteum is thickened and consists of an outer dense layer, a thickened fibro-elastic layer and a thin osteogenetic layer. Bud-like processes of the osteogenetic layer are growing inward from the periosteum. A calcified matrix forms irregular indented tapering processes. In most areas there is seen a layer of bone-matrix upon the surface of these trabeculæ. Spaces between these processes are filled with marrow containing principally fat and erythropoietic tissue, with a small amount of myeloid tissue and blood vessels. The picture is that of the well advanced development of spongy bone. Specimen No. 3: The picture is the same as that of specimen No. 1 but bone development seems more advanced, i.e., there is more bone matrix. In fragments Nos. 2 and 4 studied, there seemed to be very little bone formation and this was unsatisfactory.[1] I would judge that there was less also from the reaction to the decalcifying solution." Signed: Regena C. Beck, M.D., Pathologist, Stuart Circle Hospital, Richmond, Virginia.

[1]Author's note.—By this the pathologist means the decalcifying solution decalcified the specimens from the dogs which did not receive splenic extract many days before it decalcified the specimens from the dogs which did receive splenic extract.

Specimens Nos. 1 and 3 were those from the dogs which received splenic extract in their diet. Specimens Nos. 2 and 4 were those from dogs which did *not* receive spleen in their diet. Both from the microscopic examination and from the time of decalcification in the decalcifying solution, it is evident that union in the dogs with splenic extract diet was better than that in the dogs without the splenic diet.

From these findings it is felt that it can be definitely said that the administration of splenic extract in the diet forwards the healing of fractures. This opinion is based upon the clinical findings in fractures (new and ununited) in the human, the roentgenological findings and the results of the study of the calcium phosphorus balance in the human and the clinical and histological findings in experimental animals (dogs). All of these points are covered in this paper.

And moreover I also believe that light is shed on the physiological action of the spleen. I have clinical, roentgenological, laboratory, and histological evidence that splenic extract which is taken orally induces calcium deposition in the callus of fractures, if it does not actually stimulate the formation of new bone (and the writer has evidence which strongly influences him in this belief).

Quoting Miwa:

Dubois Raymond once said that the spleen is an inexplicable organ. His word holds good even today, for the functions of the spleen are so diverse and so indefinite that, although so many scholars have reported their findings about this organ, few, if any, of their theories have so far been generally accepted. Of late years, however, the belief that the spleen may be an endocrine organ has steadily gained ground, but little experimental evidence has been offered to support the view that the spleen is an active endocrine organ. Dominici, Pel Port, Pearce, Nathan B. Eddy, Downs Adrey and Nathan B. Eddy, Julius Mayor and Moncorps, Belak and Saghi, Elex Brinchman, Hirschfeld Hans and Walter Fabisch, S. G. Sakharoff, Toda, Oda, Hamazaki, In Inchi-zen, Ninomiya, Ohashi and Watenabe, Stschedrowitsky and Minkow and Lopatin, Stschedrowitsky and S. A. Seltzen, Farkas and Tangle, Inamura, Tokumitsu, and Toyoda and others have all commented on the subject. Their theories, however, are chiefly based upon such clinical symptoms as collapse after splenectomy or upon biological experiments with splenic substances, and only those published from our laboratory, are based on experiments such as removing and transplanting the spleen in series of animals. In order to prove convincingly that a specific organ is endocrinal, it is not only necessary to carry out such experiments as the above but it is also important to ascertain whether or not there is a splenic substance in the lymph stream or in the venous blood that would carry out any secretion or excretion from that organ, and, if there is, to observe how far this substance can control definite symptoms that develop after the removal of the organ. If such a substance exists it should be chemically isolated. The present studies have been carried out on this principle, and I have some significant facts to report.

Fig. 1. Fig. 2.

Fig. 1. Case 1. Ununited fracture of tibia and fibula, at the end of 11 months. Note that there is practically no evidence of healing in this fracture.

Fig. 2. Case 1. Roentgenogram taken 7 weeks after bone graft and splenic extract treatment was started. The abundant callus and healing are quite remarkable.

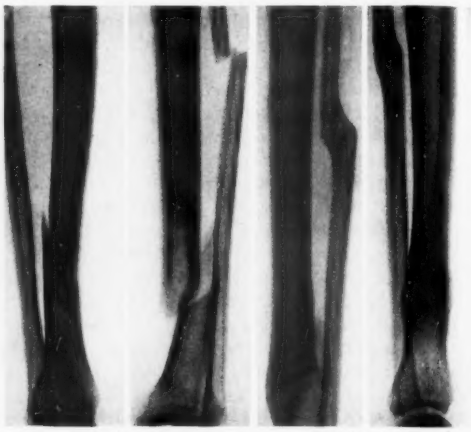

Fig. 5. Fig. 6.

Fig. 5. Case 3. Roentgenogram taken 1 year after original accident, showing no attempt at healing.

Fig. 6. Case 3. Roentgenogram taken 10 weeks after splenic extract treatment was started.

His (Miwa's) experiments showed that increase of splenic hormone causes decrease of serum calcium. Splenectomy causes increase of serum calcium. Increase of parathyroid hormone causes increased serum calcium and removal of parathyroids produces a fall in serum calcium. The increase of thymus hormone produces a fall of serum calcium and a decrease of thymus hormone produces an increase of serum calcium. While the writer has found no change in serum calcium upon the administration of splenic extract orally, the change in the calcium phosphorus retention definitely shows that there is an effect upon the calcium in the tissues (Table I). The calcium phosphorus retention studies bear out the roentgenological and histological studies that calcium is deposited.

Fig. 3. Fig. 4.

Fig. 3. Case 2. Roentgenogram taken 1 year after fracture shows very little attempt at union.

Fig. 4. Case 2. Roentgenogram taken 1 month after bone graft and splenic extract treatment had been started. This film shows a startling deposition of calcium.

Referring back then to the healing of fractures, the writer does not believe that the administration of spleen will make all fractures heal, but in the absence of other cause of non-union, he does believe the administration will help in a majority of cases to produce union, and that the cause of non-union in such cases is probably a low calcium phosphorus retention, if not actually a negative one. He also believes that the cases of tuberculosis of the bones and joints and cases of osteomyelitis that do not do well, other things being equal, have a low calcium phosphorus retention, that they will improve on splenic extract diet and that they do this because of the stimulation of calcium retention in the tissues.

Table I represents the effect of splenic extract diet upon the calcium and phosphorus retention in 3 cases. Of these 3 cases, Number 3 represents

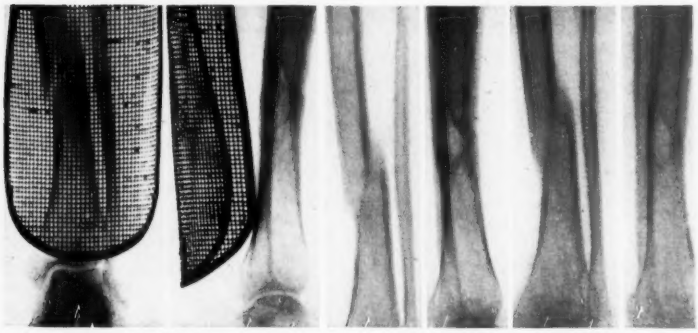

Fig. 7. Fig. 8. Fig. 9.

Fig. 7. Case 4. Roentgenogram taken 7 months after original accident. No attempt at healing.

Fig. 8. Case 4. Roentgenogram taken 11 weeks after splenic extract treatment was started.

Fig. 9. Case 4. Roentgenogram taken 13 weeks after splenic extract treatment was started. Union is obviously very firm.

TABLE I

	Calcium retention		Phosphorus retention	
	Before	After	Before	After
1	0.484	0.879	0.437	0.860
2	0.109	0.790	0.168	0.818
3	0.235	0.770	0.259	0.945

Case F.8, S.V.-2, of the series described above. The 3 cases whose calcium retention and phosphorus retention are given are cases of non-union, and it would appear that the retention in these cases was low and that it approached the normal under the splenic extract diet. It is entirely possible that this is the type of non-union case that the splenic extract diet will help most, and again it is possible that the non-union in these cases may be explained by the low calcium-phosphorus retention.

Case F.1, S.V.-2. Male, white, 64 years of age. Patient had ununited fracture of tibia and fibula, left; duration of the non-union 11 months. When patient was seen by the writer, he was using a walking splint which he had been wearing for 5 months. Roentgenogram at this time showed no attempt at union in the tibia or fibula. Physical examination was negative. Complete laboratory work, including all blood chemistry, was carried out in this case, and nothing abnormal was found. Patient was put upon splenic extract diet immediately after operation, which consisted of a massive sliding bone graft of the left tibia. He wore a plaster cast for 7 weeks, at which time union was very solid. Splenic extract diet was continued for several weeks following this, as patient seemed to have a definite calcium deficiency of the bones.

Important points in this case are that at the time of the operation, the cortex of the tibia was found to be of egg-shell thickness. Union took place in 7 weeks, and upon the splenic extract diet in a few weeks following this the tibia had regained an almost normal appearance in the roentgenogram, indicating definite calcium deposition. This patient was followed by the writer for a period of 10 months.

Case F.2, S.V.-2. Female, white, 15 years of age. Patient had an ununited fracture of the femur, right, for 1 year. Roentgen-ray examination showed only a slight attempt at union of the fragments. Physical examination was negative. Complete laboratory investigation was carried out upon this patient, and it was found not to have been altered materially. Following the operation, patient was immobilized in a plaster spica and splenic extract diet was started. Plaster was removed altogether in 3 months, with good union. Union was so solid that it was safe to manipulate the knee 4 months after the original operation in order to break up adhesions which had formed from long immobilization during her long non-union. Splenic extract was continued for 5 months.

Important points in this case are that with only a small intramedullary graft to hold the fragments in position, firm union immediately took place, and in addition there was a very startling calcium deposition about the site of the fracture, as will be seen in the roentgen-rays. This patient was followed by the writer for a period of 13 months.

Case F.3, S.V.-2. Male, white, 29 years of age. Patient had ununited fracture of the tibia and fibula, right, for 1 year. Roentgen-ray showed practically no attempt at union. Physical examination was negative. Union began 3 weeks after splenic extract diet was started and continued progressively without retrogression. The patient went back to work, doing full farm work, 3 months after splenic extract diet was started. Splenic extract diet was continued 3 months.

Important point in this case is that the healing of the fracture, after the beginning of the splenic extract diet, was almost perfectly serial, as will be

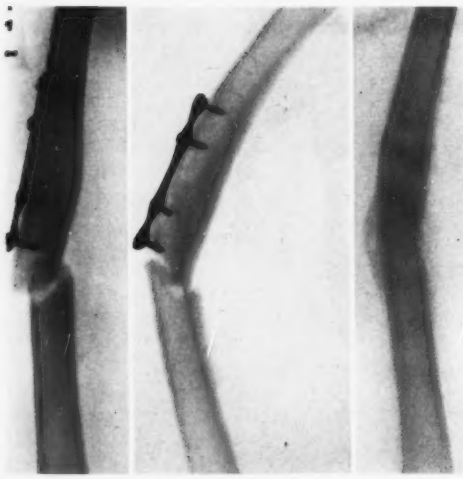

Fig. 10. Fig. 11.

Fig. 10. Case 5. Roentgenogram taken before splenic extract treatment was started. In this film may be seen the ununited fracture which had persisted for a year. It also shows a steel plate which bridges an old fracture which the patient had sustained years previously, and which also had healed with difficulty. For that reason the femur had been plated. The second fracture has occurred at the distal end of the plate.

Fig. 11. Case 5. Lateral roentgenogram of fracture taken 6 weeks after splenic extract treatment was started.

seen from the roentgen-rays. Patient was followed by the writer for a period of 6 months.

CASE F.4, S.V.-2. Female, white, 24 years of age. Patient had ununited fracture of tibia and fibula, right, for a period of 7 months. Roentgen-ray showed little or no attempt at healing of the bone. Patient had been immobilized in a plaster for several months, but was wearing only a

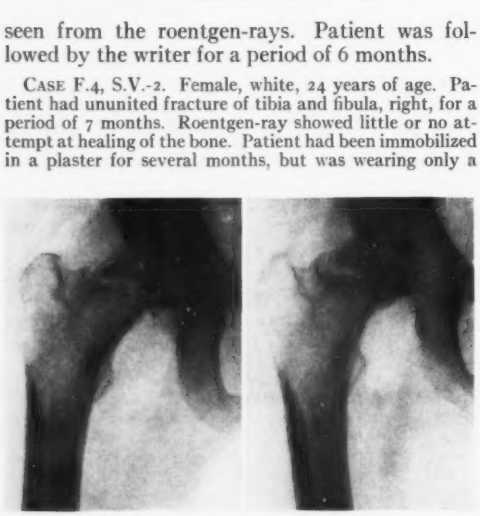

Fig. 12. Fig. 13.

Fig. 12. Case 6. Roentgenogram taken 7 months after original injury.

Fig. 13. Case 6. Roentgenogram taken 80 days after splenic extract treatment was started.

Fig. 14. Fig. 15.

Fig. 14. Case 7. Roentgenogram taken 2 months after fracture, shows malposition of fracture with a great deal of débris (later confirmed at operation) and very little callus.

Fig. 15. Case 7. Roentgenogram taken 4 weeks after operation and starting of splenic extract treatment. Healing appears to be quite unusual.

light aluminum splint when referred to the writer. Physical examination was negative. Complete laboratory investigation was carried out upon this case, and it was found not to have been altered except to have had a slight fall in the blood sugar from 98.0 milligrams to 96.0 milligrams. Patient was put upon a splenic extract diet, and from the third week healing of the bone definitely began and continued without abatement. In a period of weeks, union was very solid and patient began to walk without support.

In this case, without treatment of any kind besides splenic extract, the bones began to heal 3 weeks after the beginning of the splenic extract diet and continued to full union. Patient was followed by the writer for 13 months.

CASE F.5, S.V.-2. Male, white, 9 years of age. Patient had an ununited fracture of the femur, left, for a period of a year. Roentgen-ray showed practically no attempt at union. Physical examination was negative. Complete laboratory investigation was carried out upon this case, and it was found not to have been altered except for a slight rise in the blood sugar, from 94.0 milligrams to 98.0 milligrams. Patient was put upon splenic extract diet for a period of 13 weeks. Solid union resulted. This patient was followed for a period of 13 weeks.

CASE F.6, S.V.-2: Female, white, 19 years of age. Patient had an ununited fracture of the neck of the femur, right; duration 7 months. Roentgen-ray examination showed practically no attempt at healing of the fracture, with apparently a low-grade osteomyelitis of the neck of the femur. Physical examination was negative. Complete laboratory investigation was carried out in this case; and, except for a rise of the red blood cells from 3,430,000 to 4,470,000, with an increase in the hemoglobin from 74 to

.8 per cent nothing abnormal was found. The white blood cells fell from 15,000 to 9,000. Patient was put upon a splenic extract diet, when healing began almost immediately, and was very satisfactory in 14 weeks.

In this case not only did the fracture heal under the splenic extract diet, but the low-grade osteomyelitis present also apparently cleared up. This patient was followed for a period of 14 weeks.

CASE F.7, S.V.-2. Male, white, 42 years of age. Patient had a fracture of the femur, right, 2 months old, which had remained in malposition during this period of time. Roentgen-ray examination showed very little attempt at union. Physical examination was negative. Complete laboratory investigation was carried out in this case, and no alterations were found. The patient was operated upon and splenic extract treatment started at once. The healing of this bone was very remarkable, as can be seen in the roentgenograms. Union was very solid in 7 weeks. Patient was continued on splenic extract treatment for a period of 12 weeks.

In this case at the end of 4 weeks the healing of the fracture was very unusual. Patient was followed by the writer for a period of 14 months.

CASE F.8, S.V.-2. Female, white, 14 years of age. Patient had fragilitas ossium, with ununited fractures of the neck of the femora. This patient had had the ununited fractures for a good many years. She has been all over the world, spending a year with Rollier, in an attempt to get the fractures healed. Physical examination was negative. Complete laboratory investigation was carried out upon this case, and it was found not to have been altered except in the important increase of calcium and phosphorus retention. The calcium retention increased from 0.235 to 0.770, and the phosphorus retention increased from 0.259 to 0.945. Patient was put upon splenic extract diet, and 6 months after its beginning not only had there been very marked deposition of calcium in all of her bones, but the non-union clinically had disappeared and from a roentgenological point of view was very much improved.

In this case healing of fractures, ununited for years, took place under the splenic extract diet, and the condition of the bones characteristic of fragilitas ossium improved. Patient was under the writer's care for 10 months.

CASE F.9, S.V.-2. Male, white, 14 years of age. Patient had a fracture of the femur, left. Physical examination was negative. Immediately after the fracture of the femur had been reduced, patient was put upon splenic extract diet, and 12 days after the institution of the splenic extract diet the healing of the fracture was quite remarkable.

In this case the splenic extract diet hastened healing to a point in which fracture of the femur in a child of 14 years of age could be considered moderately firm at the end of 12 days. This patient was kept on a splenic extract diet for a period of 12 weeks. Patient was under the writer's observation for 5 months.

SUMMARY

1. Splenic extract diet would appear to hasten the healing of fractures, both fresh and ununited.

2. Splenic extract diet may induce an increased calcium retention which might explain at least one of the functions of the spleen.

Grateful acknowledgment is made to the following: Rolland J. Main, Ph.D., assistant professor of physiology and pharmacology, Medical College of Virginia, who assisted with the animal experimentation; C. Paul Reed, M.D., of the Indiana (Pa.) Memorial Hospital, who kindly collected data upon 2 cases for the writer; C. Braxton Valentine, biochemist of Valentine's Meat Juice Company, Richmond, Virginia, who generously furnished the material used in these studies.

BIBLIOGRAPHY

1. BARR, JOSEPH S. The treatment of surgical tuberculosis with splenic extract. J. Bone & Joint Surg., 1934, 16: 173.
2. BAYLE, J. C. L'opothérapie splénique. Traitement de choix de la tuberculose. Presse méd., 1925, 33: 1266.
3. Idem. L'opothérapie splénique. Traitement general de la tuberculose. Rev. gén. de clin. et de thérap. (J. Practiciens), 1931, 45: 101.
4. FLIEGEL, OTTO. Milzverfuetterung bei Gelenktuberculose. Deutsche med. Wchnschr., 1928, 54: 2053.
5. Idem. Calf-milk diet in the treatment of suppurative tuberculosis of joints. J. Bone & Joint Surg., 1930, 12: 788.
6. MIWA, TARO. J. Med. College in Keijo, 1931, 1: No. 5.
7. Idem. Studies on the splenic hormone, especially on its rôle in calcium metabolism.[1]
8. WHEELDON, T. F. Splenic extract treatment of bone and joint tuberculosis. J. Bone & Joint Surg., 1933, 15: 337.

[1]From the photostatic copy of the article made by the New York Academy of Medicine.

ELONGATION OF THE PARTIALLY CLEFT PALATE

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IN the repair of cleft palates one goal should be to obtain the best possible function of the soft palate. This will require pliable tissue, sufficiently long to meet the posterior wall of the pharynx (Passavant's pad) in the sphincter-like action of this region that closes the opening between the nose and throat. Although operations may be well executed and the palates may appear normal after operation, it is extremely exceptional that perfect speech is obtained. This persistent speech defect is probably due to a leak of air into the nose which may occur if there is an opening left of only a millimeter.

In efforts to insure complete closure, methods have been described for gaining length in the palate, or for carrying the posterior pharyngeal wall forward. These procedures have been completely summarized by Dorrance in *The Operative Story of Cleft Palate* and need only mentioning here.

Elongations have been done by freshening the edges of the posterior pillars, detaching them low down in the pharynx and then suturing them together in midline, thus extending the palate behind the uvula; this has effected good results in many cases, but tissue that is normally a tensor of the palate is changed around so that the levators pull it up in closure of the opening. Blair has put rectangular flaps from the cheeks across the palate after it has been dissected backward, but the procedure is somewhat formidable for the gain involved. Gillies and Fry have described a backward dissection of the palate with an apparatus to hold a skin graft on the raw surface, the resultant opening into the nose in the front part to be closed by an obturator.

Some think that in complete clefts an operation of the Dieffenbach principle may be executed to allow moving backward of the entire palate, but, if any great displacement is done, a hole persists in the front part of the palate. Others have even sacrificed the closure in front in order to have the tissue available posteriorly and have then used obturators for the anterior opening or have brought in flaps from a distance.

After closure of the palate, several surgeons have directed their attention to carrying the posterior pharyngeal wall forward: by reefing it forward, by the use of a submucosal prosthesis, and, by rectangular mucous flaps dissected free from the pharynx and attached to the soft palate (Padgett and Wardhill). Any of these measures, especially the reefing forward of the posterior wall can be added to this procedure if the operator so desires.

Palates that are cleft only through the soft tissue or on up, part way through the bone, may have actually less tissue for repair of the soft palate than those with complete clefts; and there are also patients with uncleft palates that are so abnormally short that speech is just as bad as though the palate were cleft. Dorrance has called this "congenital insufficiency of the palate." It is in this group that the most direct attempts have been made for actually lengthening the palate, by moving the whole of the soft tissues backward and still having the bony palate in front to separate the nose and the mouth. Dorrance's procedure which he calls the "push-back operation" is probably the best known. The essentials are that a delayed flap of the entire covering of the bony palate is made except that the major palatine arteries are sacrificed. At a later operation the muco-periosteum is again raised from the bone and the whole mass is "pushed back" so that the anterior edge of the flap may be anchored as far back as the posterior bony edge. The cleft is closed and the anterior denuded bone is left to heal over.

AUTHOR'S TECHNIQUE FOR LENGTHENING THE PARTIALLY CLEFT PALATE

Our interest in the problem of obtaining the longest possible palate has fluctuated with the results obtained with various procedures, but since September, 1931 (after Dorrance's first report of his technique), we have used the procedure outlined here. The principle is that a direct flap of practically the entire palate is raised completely free from the bone and is immediately set back so that the anterior free edge is anchored clear back at the posterior edge of the bone. The major palatine arteries are definitely preserved and left to supply the palate flap. The palate is allowed to heal here, the bony palate to cover completely with epithelium and, at a second operation, the palate cleft itself is closed.

First operation. An incision is made across the surface of the anterior pillar, over the ramus and onto the maxillary tubercle; it is then carried

Fig. 1.

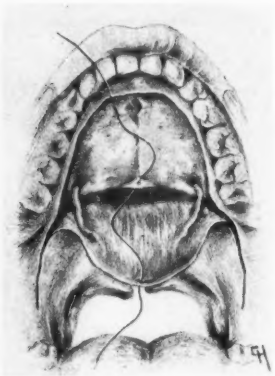

Fig. 2.

Fig. 3.

Fig. 1. Line of incision and beginning elevation of mucoperiosteum.

Fig. 2. Diagrammatic representation of palate completely detached from bone, both major palatine arteries intact, and preservation of a band of nasal mucosa to which the palate is attached with the first suture as shown.

Fig. 3. Detail diagram of deep separation of the soft tissues, exposure of the hamulus, freeing of the palate aponeurosis in this area behind the artery, section of the tensor tendon.

entirely around the palate against the alveolus and out over the opposite side (Fig. 1).[1]

An elevator is used to detach the mucoperiosteum completely from the bone, and the arteries are carefully preserved. When the posterior edge of the bone is reached, the nasal mucosa is carefully opened and a narrow edge is left attached to the bone to be used for the anchoring sutures that are put in later (Fig. 2). The elevator is put behind the arteries and the space down to the hamulus and pterygoid plate is opened so that the surface and deep soft tissues throughout the entire extent of the incision may be freely mobilized. The tensor muscle may be divided at the hamulus and the dissection of the aponeurosis from the posterior edge of the bone is completed so that the entire mass of palate tissue is held by the remaining uncut surface over the pillars, the major arteries and the levators. At this stage, in spite of the very free dissection, it is interesting to note that the levators are still active (Fig. 3).

The arteries are then elongated by carefully stretching them from their foramina and slightly separating them from the raw surface of the palate. We are convinced that this procedure can be successfully carried out as we have done it throughout this series, and we do practically the same thing in repairing total clefts.[2]

When the palate is quite free and movable the anterior cut edge is sewed clear back at the posterior bony edge, being anchored, with a horsehair suture, to the little flap of nasal mucosa that is left attached here. The lateral free edge of the flap is then anchored at the maxillary tubercle on each side and one or two more sutures may be inserted (Fig. 4).

The tissue is usually somewhat humped up, but it is definitely longer and the halves of the soft

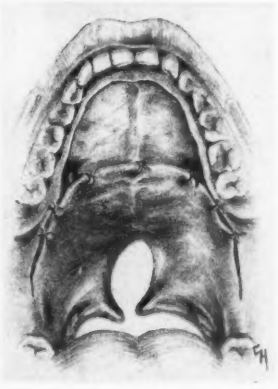

Fig. 4. Completion of first stage: The palate has been set back and anchored with horsehair sutures as shown. Several layers of iodoform and balsam of Peru gauze are placed smoothly over the exposed bone and will be retained without sutures for several days.

[1] All illustrations are diagrammatic; drawn as though the palate were viewed from below instead of through the open mouth.

[2] Blair, V. P., and Brown, J. B. The Dieffenbach-Warren operation for closure of the congenitally cleft palate. Surg., Gynec. & Obst., 1934, 59: 309-320.

Fig. 5.

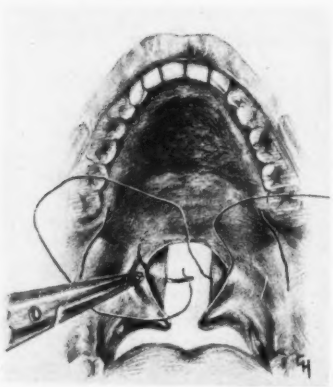

Fig. 6.

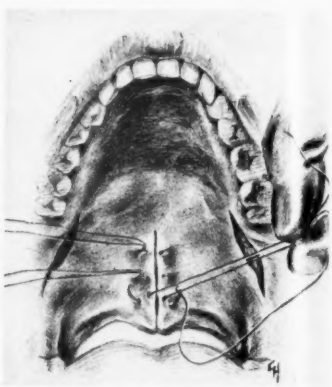

Fig. 7.

Fig. 5. Beginning of second stage: New openings through the former lateral incisions may or may not be thought necessary. The edge is trimmed off from the tip of the uvula up into the palate substance about .2 millimeters.

Fig. 6. A deep stay suture is usually placed to engage a good bulk of tissue. This may be of catgut and tied on the nasal surface or it may be of non-absorbable material and brought out into the mouth. Extra muscle and nasal mucosa sutures may be put in at this stage.

Fig. 7. Closure of the cleft with vertical mattress sutures of horsehair. The closure is carried entirely around the uvula and then up onto the nasal surface with fine catgut sutures.

palate may be lying in contact with the posterior wall. The anterior defect is covered smoothly with a pack of balsam of Peru and iodoform gauze, and no sutures are necessary to retain it.

If indicated, a tonsillectomy and an adenoidectomy is done at the start of this operation.

Recovery is usually prompt and the patient can leave the hospital in 3 to 7 days. The pack is removed about the sixth day, and repacking is occasionally necessary for bleeding.

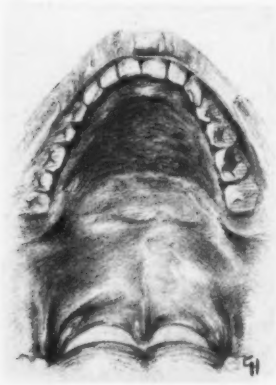

Fig. 8. Completed and healed palate: Set back the distance of the original exposed bone shown in Figure 4, minus the folding of the soft tissue and the contraction in healing. It is not possible to tell by looking at the palate whether or not it completely closes the nasopharynx, but, of course, the greater its length, the better is its chance of doing so, provided the levator muscles are functioning.

Complete healing of epithelium over the bony palate occurs in 20 to 30 days, and is practically normal in appearance except that rugæ are not present. At this stage the soft tissues may be somewhat humped up from side to side just behind the edge of the bone. The actual lengthening might be said to be the difference between what tissue is used in this humping up and the total distance the edge is set back. This distance may be as much as 2 centimeters, and is the space between the anterior incision to the posterior edge of the bone. Improvement in speech is usually already noted even though the cleft is not completely closed.

Second operation. The cleft in the palate is closed as desired, either by simply freshening the edges and suturing them or by first undermining through new lateral incisions to gain any necessary mobilization (Figs. 5, 6, and 7). This stage may frequently be combined with the first stage, so that only 1 operation is necessary.

RESULTS OF TREATMENT AND QUALIFICATIONS OF THE PROCEDURE

By this time I had hoped to report on more patients; however, over the 5-year period, observations even on this small group may be worthy of evaluation.

1. In 53 operations performed on 32 patients, there have been no deaths; 25 of these have shown excellent results and the 7 others have not had the final step completed.

2. Hemorrhage occurred from the incisive canal, so severe in one adult that operation was discontinued and completed at a later date when more attention was paid to her pre-operative care. Hemorrhage occurred in one patient following the removal of the pack but was easily controlled with another pack.

3. If there is interruption of the blood supply of the major arteries either when operation is done, or if a previous operative attempt has sacrificed them, it will perhaps be best to revert to a "delayed flap" type of operation, as described by Dorrance rather than to set the palate back at the first operation. In one patient there was a small slough anteriorly due either to sacrificing an artery inadvertently, or to its being kinked in its new position.

4. Palates badly scarred from former operations cannot be expected to submit to manipulation as readily as unscarred ones.

5. If there is a bony defect extending up the center of the palate, very careful separation of the flap should be done to preserve the nasal mucosa, otherwise a hole will be left anteriorly. The limits of the bony edge or the possibility of a long, narrow central cleft can be determined with a fine hypodermic needle if desired before operation. In one of the 6 uncompleted cases, an attempt was made to lengthen a completely cleft palate that had already been closed, and a defect resulted anteriorly that may require an obturator.

6. If the operation is done too early in life, any tooth buds outside the alveolus may be damaged, the same as in any other operation, as has been emphasized by Logan and Kronfeld. Eight months is the age of the youngest in this group and operation was done only at the insistence of the parents.

7. One patient who had a neuronitis and whose mentality did not offer much hope of success, developed such excellent speech that he was able to be understood in reciting a short poem to a large audience.

8. All of the older patients have expressed great appreciation and have felt definite improvement in speech. One western ranch hand, undoubtedly the subject of much ridicule, stated that he was able for the first time really to get by with his work, and to direct others at work.

9. Both stages have been completed in one operation but the two separate stages are relatively easy ones for the patient.

10. One patient with a very short soft palate cleft that had been closed elsewhere was set back as far as possible with preservation of both arteries, and when, after it had completely healed, it was found that still further length could be gained, it was set back again and the arteries were definitely preserved at this time also.

11. In a girl of 10 years there was practically no bony palate whatever and a corresponding lack of soft tissue with extreme width of the cleft so that it did not seem that any type of closure could be obtained. However, in this patient, even the short setback obtained at the first operation made subsequent closure of the cleft possible and, though the final palate was short, there was marked improvement in the child's speech and eating.

12. A possible objection to this procedure is that the resulting raw nasal surface may contract and shorten the palate secondarily, but so far we have not noted this as being important enough to try to cover the raw surfaces with skin grafts.

13. This procedure seems to be adaptable to a small percentage (possibly about 20 per cent) of the total cases, but, as its steps can be changed around, or combined in one operation, and, as the first stage may be used to elongate partial clefts already closed, its usefulness may be increased. It is also possible that palates with total clefts that have been closed can be lengthened, either by preserving the nasal mucosa anteriorly to permit of spontaneous healing, or by using an obturator on a dental prosthesis.

14. No claim is made that perfect closure is to be routinely expected but it is thought that results thus far have been very encouraging. Speech-training is considered as important as in any other type of palate closure.

LOCALIZATION AND EXTRACTION OF FOREIGN BODIES WITH THE AID OF COLORED ROENTGEN OPAQUE OIL[1]

JOHN D. ELLIS, M.D., F.A.C.S., CHICAGO, ILLINOIS

IN civilian practice no surgeon has the opportunity to acquire expert skill in the localization and extraction of foreign bodies. He is, however, expected by the laity to be able to remove a foreign body from an extremity at one operation and with ease. A failure to do so at one operation is damaging to surgical reputations.

It is evident that most civilian hospitals are not likely to be equipped with elaborate x-ray surgical tables, designed for this special purpose, or that the surgeon who is called upon only occasionally to remove a foreign body will familiarize himself with the double image or the intersecting axes method of visualization or such instruments of precision as the Hirtz (3) or the Saissi (1) compass, successfully employed during the latter part of the World War by experts in extraction.

Any simple method of precision is an improvement over a haphazard approach to the foreign body. We have combined the so called surface localization of Viallet with a precise means of internal anatomical localization, using a contrast medium of iodized or bromidized oil colored with one per cent oil soluble green dye.[2] The oil can be visualized in the tissues by roentgenograms and its exact relation to the foreign body determined. However, unless this oil is stained with a vivid dye contrasting with the red of the muscle or the yellow of fat, it cannot be located in the tissues during the operation. Therefore, a brilliant green fat soluble dye is added to the oil. The absence of inflammatory reactions has been demonstrated by experimental injections of this preparation in human subjects during operations and into the muscles of dogs.

We first used methylene blue, which is not oil soluble, dissolved in sterile glucose syrup and shaken with bromidized olive oil into an emulsion. This preparation is also useful for injecting sinuses, as it is radiopaque, and when the sinus is to be dissected out is not found to permeate surrounding tissues, as commonly occurs with an aqueous solution of methylene blue.

The method proposed can be employed in any hospital provided with an x-ray equipment and operating room. Suitable wire screens can be made in a hardware store. These (Fig. 1) were devised by Dr. Mitchell S. Corbett of Chicago and are of various sizes. The largest, 8 by 18 inches with a ¼ inch mesh, is employed on the shoulder, buttock, neck or thigh; the smallest, 1 by 1½ inches with a ⅛ inch mesh, on the finger. These are bent to true right angles.

TECHNIQUE OF LOCALIZATION

Preliminary films are first taken to be used as guides in determining the position of the patient on the operating table and the best position for the right angle screen to be applied. The patient is then placed on the operating table and securely fastened to prevent movement. If roentgenograms are to be taken in a separate room, a wheel cart is employed from which he is not moved after the localizing roentgenograms are made. The operation is performed without moving him from the table or wheel cart or changing him from the position in which the localizing films were made.

If bodies are to be removed from the spine, from the dorsum of the neck or an extremity, the patient must be immobilized and anesthetized in a prone position.

Next, the skin is sterilized and the sterile right angle screen fastened to the part by a half hitch with tape or cord (Fig. 2).

A roentgen film is taken of each side of the wire screen with the tube centered and the "normal ray" at right angles to the flat surface of the screen. This can be checked with a carpenter's square. The distance of the tube should be a meter or more, if this is practical. This distance insures a more nearly orthogonal projection of the film image.

From these films the surface localization can be accurately determined by counting off the interstices of the metal screen on the film image and on the skin. The body is outlined on the skin with a dye or metal points which are left in place until the operative incision is made.

The depth can be measured on the film of the other surface of the screen. Thus, the surface localization can be determined on either film and the depth measured on the other.

A fine needle of appropriate length, as measured on the metal screen, is introduced through the surface projection of the foreign body on one plane of the screen and at right angles to it. Thus

[2]Supplied by Abbott Laboratories.

[1]From the Department of Surgery, Northwestern University Medical School.

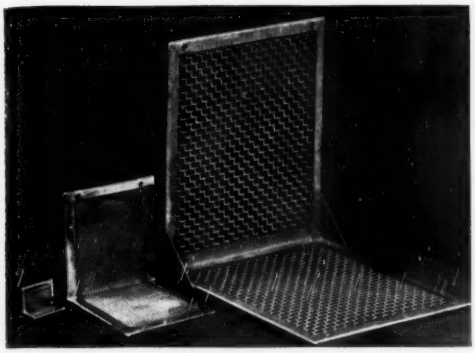

Fig. 1 Various sized screens for use in "surface localization."

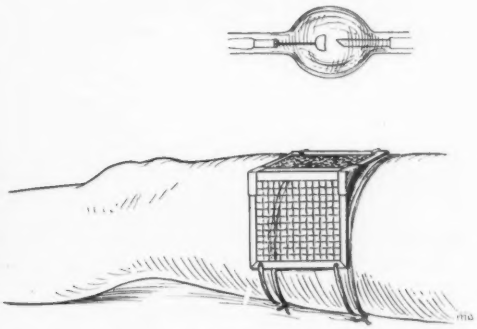

Fig. 2. Schematic drawing of position of screen and roentgen tube.

the approach on the foreign body is easily made. This introduction is, of course, a matter of skill as well as precision. A few drops of the colored oil are introduced at the site where we expect the foreign body to be located. As the needle is withdrawn a fine trace of colored oil is left along the path by gentle pressure on the syringe. This may serve as a guide in the surgical approach to the deeply injected oil.

Another set of films is taken and the relation of the colored roentgen-ray opaque oil to the foreign body can be determined. If the first attempt is not successful and the deposition of oil is not in close proximity to the foreign body, the operation can be postponed for a few days, until the oil is dispersed, and another attempt to obtain internal localization by means of the oil can be made.

While several experts during the World War experience enthusiastically recommended needle localization or the use of skewers, placed in the part under fluoroscopic guidance, this requires much more experience than one who has not undertaken it would believe. Puncturing a part at random in a dark room is not without the danger that the needle may strike a nerve or large vessel. Furthermore, a needle inserted directly in the path of the "normal ray" appears only as a point under the fluoroscope. This difficulty, of course, may be obviated by using an angulated needle. It is much more laborious to reach the foreign body in a direction oblique to the ray and more perplexing to tell whether the point of the needle is nearer or farther away from the roentgen tube than the foreign body which is sought. If local anesthesia must be introduced each time before this attempt is made with alternate changing from dark to light during the application of the anesthetic, the insertion of the needle is rather confusing to surgeons. For these reasons the right angle screen method with stained opaque oil has been devised.

However, if a foreign body can be localized with a hollow needle under the fluoroscope, the anatomical localization can be quickly established by introducing the colored oil and checking this thereafter with roentgenograms in two planes.

We prefer general to local anesthesia whenever possible, as local anesthesia often distorts the topography of the part.

OPERATIVE TECHNIQUE

The screen should be removed by cutting the tape holding it after the patient is anesthetized. Firm fixation of the part to be operated upon during the induction of anesthesia and complete muscular relaxation by anesthesia are both important considerations. Duval quotes the example of a bullet located in the adductors of the thigh which changed its position as much as 8 centimeters according as the muscles were contracted or relaxed and which was missed twice in operation.

A Martin bandage should either be applied before the roentgenograms are taken or else dispensed with entirely.

Before the skin incision is made and as each fascial plane is approached, points on either side of the contemplated incision line are seized with Allis forceps and lifted so that the pressure of the knife will not displace a movable body beneath. Wide exposure and a minimum of sponging is desirable. A single foreign body can be found in the colored oil. A collection of minute fragments or an encapsulated body can be removed by dissecting out the colored oil *en masse*.

Glass fragments visualize easily in roentgenograms if the image is projected clear of the bones (Kahlsdorf). Barium and lead glass particles, less than 2 millimeters in diameter, have been localized anywhere in the body by Lewis in an exhaustive experimental study.

Our method is intended particularly for use on the extremities. Some regions present unusual difficulties in localization.

Foreign bodies in the buttock and about the hip region are difficult to extract for two reasons: first, because exact radiological localization is difficult, and second, because the loose tissues of the buttock make the depth from the fracture surface, the surface of surgical approach, variable, depending upon the amount of pressure with which the localizing screen is applied. Leaving a trace of colored dye along the needle wound during extraction aids in obviating the latter difficulty.

The direction of surgical approach on the deep lying foreign body depends on whether it is situated above or below the neck of the femur, within the bone itself or within the joint capsule.

The shoulder and axilla are difficult to study roentgenologically for foreign bodies because of the necessity of taking one view entirely through the chest in studying the subscapular and deeper parts of the axillary space. This makes distortion of the image of the foreign body more difficult to avoid. The surgical approach to the axilla is not so embarrassing once the oil has precisely localized the region to be explored.

REFERENCES

1. Albert-Weil, E. Localization et extraction des projectiles. Paris méd., 1916, 19:129-135.
2. Duval, P. Technique operatoire de l'extraction des projectiles. Rev. de chir., 1916, 51: 1-19.
3. Hirtz, E. J. L'examen radiologique des blesses et la recherche des projectiles. Arch. de méd. et pharm. mil., 1916, 65: 499-521.
4. Kahlsdorf, A. Ein Hinweis auf die Roentgenologische Darstellbarkeit von kleinsten Glassplittern als Fremdkoerper. Deutsche med. Wchnschr., 1933, 59: 1286-1287.
5. Lewis, R. W. Roentgenographic study of glass and its visibility as a foreign body. Am. J. Roentgenol., 1932, 27: 853-857.

THE TRANSFER OF TUMOR CELLS BY THE SURGICAL KNIFE

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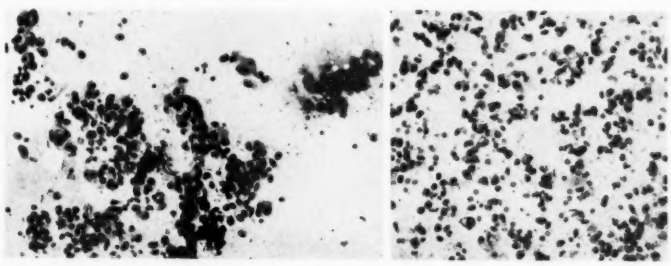
A NUMBER of surgeons discard the knife after it has been used for the removal of a biopsy of a malignant tumor and continue the radical operation with another knife or with a second set of instruments. This practice, however, is not universal and the same instruments still are used for both the removal of the biopsy specimen and for the radical operation. The former practice is primarily based on the fact that occasionally the tumor recurs along the operative scar at the site of the radical operation.

This communication is the result of the examination of the material which adheres to the blades of knives used for obtaining biopsies of tumors, particularly breast tumors. All the knives with which various types of malignant tumors were incised, were examined shortly after they had been used. Either direct smears were made from the respective blades or the blades were washed with a small quantity of saline and smears were made from this suspension. The smears were stained with hematoxylin-eosin according to the method recently described by Martin and Ellis in their study of aspiration biopsies. Also, iron hematoxylin preparations of the smears were used satisfactorily.

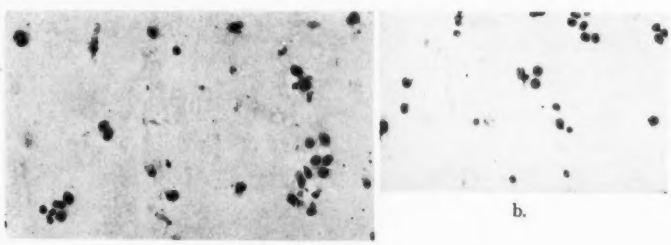
Invariably, smears which were made from the material on the knives used to cut through the tumors showed tumor cells. In some instances, the tumor cells were so abundant that at low magnification their numbers were comparable to that of erythrocytes on a blood smear of average thickness. Also, smears which were made from material on the knives used for removal of the primary tumor for biopsy before the radical breast operation was performed, revealed tumor cells.

From this study, it seems that every biopsy carries with it the danger of transferring, and pos-



a. b.

Fig. 1. Smears made from blade of knife which was used for cutting through carcinoma of the breast. (Iron hematoxylin-eosin preparation; a, ×250; b, ×200). Note the clumps of carcinoma cells in a and the individual tumor cells in b.



a. b.

Fig. 2. Smears made from blade of knife which was used to excise carcinoma of the breast. (a, Iron-hematoxylin-eosin preparation; ×250; b, hematoxylin-eosin preparation; ×250).

sibly transplanting, tumor cells into healthy tissue. By means of supravital dyes (Hickling), reasonable evidence was obtained that the tumor cells on the knives were still viable. One factor, therefore, essential for the propagation of tumor was present, namely, living tumor cells. Whether or not these tumor cells actually encountered suitable environment or "fertile ground" essential to their growth is the other factor which, of course, cannot be ascertained. The potential danger of transplanting tumor cells by the knife is proportional to the number of tumor cells attached to the knife. Hence, the incision into the primary tumor carries a greater danger than the incision about the primary tumor.

The facts here presented may also explain "the special danger pertaining to the incision of the tumors" (Hellwig) but from a different point of view than the author implies. Whereas Hellwig speaks of stimulation of growth and dissemination of tumor cells through the blood and lymph vessels, these dangerous sequelæ may be explained by the dropping of viable tumor cells which may actually be transferred into the blood vessels or tissues by the dissecting knife. The perilous effect of tumor cells adherent to the blade of the knife is clearly brought out by Bloodgood's statement, gained by experience, which stresses the danger in excising a cancer of the breast without the use of the cautery and then waiting longer than 2 weeks before the radical operation. Greenough, Bland-Sutton, Bainbridge, and others are of the opinion that one of the most vital principles of surgery in malignant disease is that cutting into cancerous tissue leads to a spread of the disease. It is apparent that this spreading of tumor cells by the knife may easily be the underlying factor which leads to the acceptance of this principle. These authors also gained this view by following up the individual patients rather than by the actual finding of tumor cells on the knife.

It is noteworthy that Rydall in 1908 stated: "A scalpel which has been used for mere incision into a cancerous growth has, as a result, cancer cells, almost invariably, clinging to the blade, and I think I can safely say that cancer cells are always liberated into the blood escaping from the incision." The viability of these cells, however, was not proved. Butlin, one year previously, remarked that the instruments which were used for the purpose of diagnosing the malignant tumors must not be used again until they have been boiled. Ewing, very recently, recommended the change of gloves and instruments after the performance of a biopsy of malignant tumors.

In view of the findings here presented, it is imperative to change the knives not only after removal of the biopsy but also after excision of a malignant tumor before a radical operation.

SUMMARY

Examination of the blades of knives used for removal of biopsies from malignant tumors or for removal of seemingly well circumscribed malignant tumors revealed a varying number of apparently viable tumor cells. These tumor cells represent a potential danger, as they may be a source of local recurrence and also of metastasis. One important source of local recurrences of malignant tumors therefore may be avoided if the dissecting knife and other instruments are discarded after the removal of the biopsy of the primary tumor before proceeding with the radical operation.

LITERATURE

1. Bainbridge, W. S. Biopsy and cancer. Med. Rec., 1917, 91: 706.
2. Bland-Sutton, J. Tumors. In W. W. Keen's Surgery, Vol. i, p. 804. Philadelphia and London: W. B. Saunders Co., 1907.
3. Bloodgood, J. Biopsy in diagnosis of malignancy. South. M. J., 1927, 20: 18.
4. Butlin, H. T. The contagion of cancer in human beings: auto-inoculation. Lancet, 1907, 2: 279.
5. Ewing, J. Biopsy in mammary cancer. Illinois M. J., 1933, 63: 482.
6. Greenough, R. B. The handling of early and doubtful cases of cancer. Ann. Surg., 1917, 66: 385.
7. Hellwig, C. A. Scientific basis of biopsy in tumors. Arch. Path., 1932, 14: 517.
8. Hickling, R. A. Vital staining of malignant cells in a peritoneal effusion. J. Path. & Bacteriol., 1931, 34: 789.
9. Martin, H. E., and Ellis, H. B. Aspiration biopsy. Surg., Gynec. & Obst., 1934, 59: 578.
10. Rydall, C. The technique of cancer operation with reference to the danger of cancer infection. Brit. M. J., 1908, 2: 1005.

AN ARTHROPLASTIC OPERATION FOR CONGENITAL DISLOCATION OF THE HIP—A TWO STAGE PROCEDURE

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THE treatment of congenital dislocation of the hip in the majority of the cases over 3 years of age is more satisfactorily accomplished by some form of open operation than by any method of closed reduction.

The method presented here is a two stage procedure and has been employed a number of times since it was first described in the *Journal of Bone and Joint Surgery*, January, 1932. Six case histories with pre-operative and postoperative roentgenograms are presented, the first of which was done in 1930 and the last over one year ago.

Briefly, the first stage consists of a thorough stretching of the muscles about the hip, subcutaneous tenotomy of the adductors, and skin or skeletal traction preliminary to open operation.

At the second stage the portion of the hour-glass, synovial membrane-lined capsule covering the head is preserved and placed deeply within a reamed out acetabulum. This arthroplastic type of operation has as its aim the actual reduction of the dislocation, the restoring of stability to the hip joint, and the preservation of a satisfactory range of mobility. To date the procedure has not been used in those cases in which it was felt closed reduction would suffice and in general one may say the best results have been obtained in children under 10 years of age.

Anatomical considerations. In the backward and upward displacement of the head of the femur that is usually found in congenital dislocation of the hip, a recognition of the relationship of the head of the femur to both the vertical and horizontal planes of the acetabulum is of essential importance. Therefore, unless the head is brought not only downward but forward, the awkward lurch in walking is not corrected.

With the primary maldevelopment of the acetabulum and upper extremity of the femur there are accompanying secondary changes in the soft tissues. As these patients begin to assume the stresses and strains of activity, the muscles and ligaments assume the brunt of the burden of weight bearing. The capsule becomes elongated to accommodate the upward and backward displacement of the head of the femur producing the so called "hour-glass" appearance and the capsular ligament over the neck and head of the femur becomes thickened. The interior of this elongated capsule is in reality a portion of the hip joint and is lined with synovial cells. The lumen of the isthmus at the contracted portion may contain the attenuated ligament teres or one may be unable to identify the teres as a definite structure and the lumen appear obliterated by fibrous tissue. At operation an excess of synovial fluid in this capsular sac about the head often can be seen.

The pelvic-trochanteric group of muscles, as well as the adductors, are contracted and act as definite barriers to reduction. For this reason the first stage of the procedure advocated has been a very beneficial preliminary measure.

While the time of follow-up with the procedure advocated is insufficient to draw any definite conclusions as to what will be the ultimate functional and roentgenographic appearance of these hips, certain observations have been noted in the patients operated upon. The hips have all remained reduced and stable with a varying degree of movement. In general it may be stated that an excellent range of movement has been obtained up to the age of 8 and in a few cases above the age of 10. By cutting through the greater trochanter a stimulation of its growth has been observed, and this in the later cases appears to have been lessened by carefully removing only a small portion of the cartilage when the abductor muscles are reflected upward during the second stage. A surgical fusion of this epiphysis at this stage might obviate this, but it has not been considered necessary to date. An increased density of the roof of the reamed out acetabulum has been a frequent finding and we must assume that the transplanted capsule about the head becomes attached to the newly formed acetabulum allowing the head to move easily within the reconstructed acetabulum. The depth of the reamed out acetabulum appeared either unchanged or in some instances even appeared to have become deepened after several years of weight bearing.

The roentgenographic development of the epiphyses has been uniform, i.e., those cases that presented either fragmentation or irregular outline of the epiphysis preceding open operation, have continued to show certain characteristics of Perthe's disease or occasionally improvement in the appearance of the contour of the epiphysis; while those with smooth outlines and

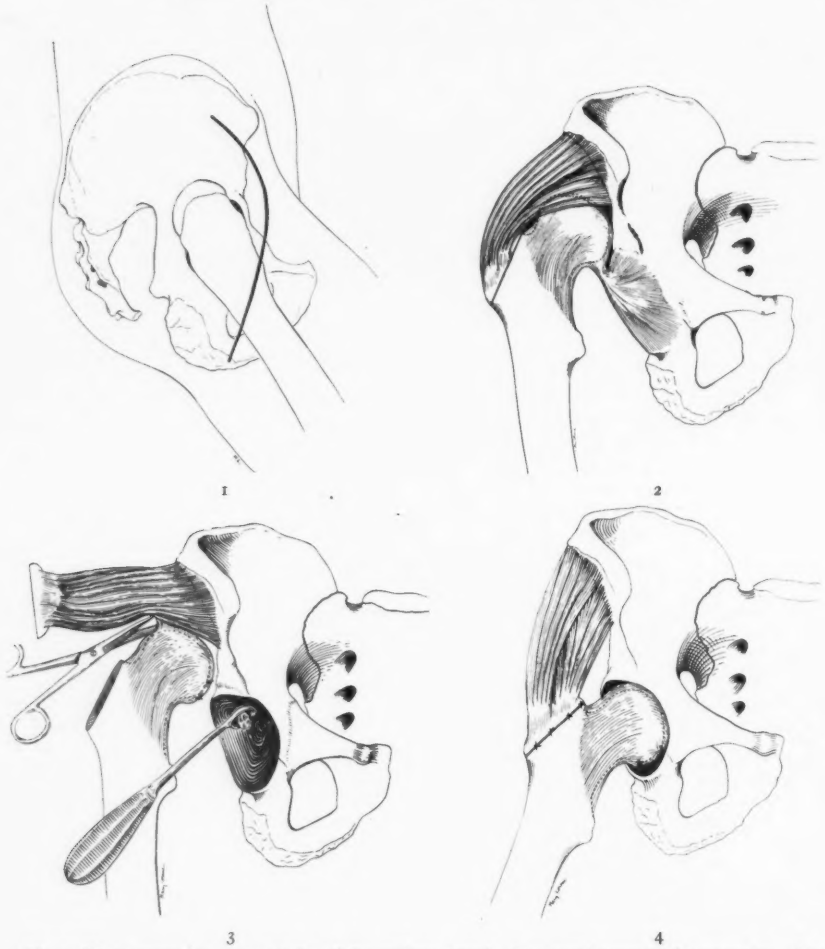


Fig. 1. Diagrammatic representation of the various steps in the second stage of the operation. The capsule is easily separated from the overlying abductor muscles and the portion covering the dislocated head carefully preserved; both being reduced into the reamed out acetabulum, without tension, as described. 1, Skin incision. 2, Diagrammatic view of hour-glass appearance of capsule. Drawing shows how great trochanter is chisled through. 3, The greater trochanter with its attached muscles retracted upward and the capsule easily separated from the surrounding structures and followed down to its isthmus. The capsule is then cut across and by several sutures made into a sac covering the head. With Doyen reamer or large curette a smooth, capacious acetabulum is made at the site of the original acetabulum. 4, The head with its synovial lined capsule is then deeply placed in the newly formed acetabulum, the greater trochanter replaced and held with several kangaroo sutures and the wound closed in layers. A long plaster spica is then applied with limb in 15 to 20 degrees' abduction.

normal structures before operation have continued their apparently normal growth.

OPERATIVE PROCEDURE

First stage. Twenty-four hours before any preliminary stretching is done, moleskin adhesive straps are applied to the affected limb extending up to within a few inches of the tip of the greater trochanter. The following day, after the moleskin has well attached itself to the skin, the dislocated hip is thoroughly stretched under anesthesia, and the adductor muscles subcutaneously

A B C

Fig. 2. Case 1, P. S., age 7 years. A, Bilateral congenital dislocated hips. B, Appearance of right hip 1 year after open operation. Hip pried into place by means of skid and without interposition of capsule. Appearance of left hip 6 months after open operation by arthroplastic method described. C, Five years later. Left hip has remained freely movable and the right hip has become practically stiff.

tenotomized. A long plaster spica is applied to the opposite side and 10 to 15 pounds of skin traction is immediately applied to the side being treated. This weight is increased gradually over a period of 2 or 3 weeks. In some cases, skeletal traction has been used. Roentgenograms are taken with and without traction to determine the actual stretching of the soft tissues obtained, and when the head is opposite the original acetabulum open operation should be done. When the maximum stretching has been obtained the plaster spica is bivalved and the hip region prepared in the usual manner, disturbing only as little as necessary the moleskin straps. The patient is sent to the operating room with the traction intact.

Second stage. In some instances the Smith-Peterson approach has been employed; though the following procedure has been found more satisfactory. A skin incision is made beginning about 2 inches behind the anterior superior spine, curving forward, downward, and then backward, as shown in the diagram, to a point about 2 inches below the tip of the greater trochanter. The rectus femoris tendon at its origin from the anterior inferior spine is identified and in some cases has been divided by zigzag tenotomy. The fascia on the lateral aspect of the thigh is divided transversely, and a portion of the greater trochanter with its attached gluteal muscles is identified, chiseled through, and turned upward. The elongated portion of the capsule of the hip joint covering the head of the femur is easily identified and separated from the surrounding structures anteriorly and posteriorly by scissor dissection (Fig. 1). When the isthmus of the capsule is reached, it is divided and the head of the bone is inspected, its shape and the presence or absence of the ligamentum teres being noted. The opening in the capsule over the head is then closed with several chromic sutures. With Doyen reamers or a large curette, a capacious acetabulum is formed, as near its original site as preliminary traction has made possible. The site of the acetabulum is further checked by identifying the triradiate cartilage in the floor of the acetabulum. Then the capsule covered head is pulled down and *without tension* placed in the deepened and reamed-out acetabulum; the abductor muscles with the attached cartilage from the greater trochanter are sutured back into place, and the wound is closed in layers. In some instances weights were reapplied, at the operating table, to the traction straps and a plaster spica, extending from the ankle to the axilla with the limb in about 20 degrees abduction, was applied to the operated limb. This traction usually remained in place for the following 2 weeks, and then the ends of the straps were cut off and plaster was applied to the foot. In the younger patients postoperative traction did not seem necessary and a long plaster spica was applied in the operating room.

The plaster is retained for 4 weeks and, after removal, active and passive movement of the limb in bed is encouraged. No weight bearing is advised for at least 3 months after open operation.

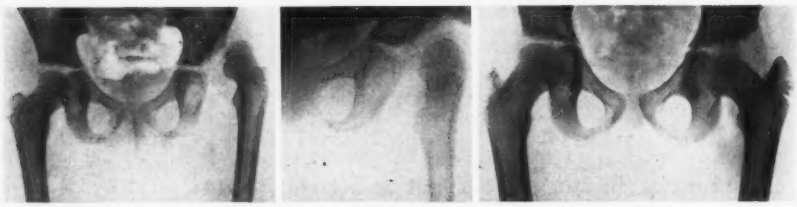
Case 1. P. S. (Figs. 2, A, B, and C). A boy 7 years of age was admitted to the Orthopedic Service at Bellevue Hospital in June, 1929. He presented the characteristic features of bilateral congenital dislocation of both hips.

December 15, 1929. The right hip was operated upon without preliminary traction and reduced with difficulty. The head was forced into a reamed out acetabulum with a skid. The result proved unsatisfactory and the hip has become increasingly stiff. As shown in the roentgenogram, the bony proliferation about the joint has continued to increase since operation.

June, 1930. The procedure here advocated was performed on the left hip. The left hip structures were stretched and the adductors tenotomized and heavy skin traction was applied, as described in the first stage of the operation. Several weeks later, i.e., June 16, 1930, the

A B

Fig. 3. Case 2, P. Z., girl 4½ years of age presenting right congenital dislocation of the hip. A, Roentgenogram taken at the end of the first stage showing the head well pulled down opposite the acetabulum. B, 3½ years postoperative. Range of movement free in all directions. Note density of acetabular rim and preservation of joint space.



A B C

Fig. 4. Case 3, A. Y., girl 6 years of age—congenital dislocation of right hip. B, roentgenogram at end of first stage. C, 2 years and 10 months after operation. Range of movement free in all directions. Note density of acetabular rim and acetabular joint space.

A B

Fig. 5. Case 4, D. K., girl 4½ years of age, presenting congenital dislocation of left hip. B, Two years and 1 month after operation. Presents excellent range of movement in all directions and no shortening. The wedge-shaped appearance of the epiphysis has persisted but the outline appears smooth and the development appears uniform.

second stage was completed. Roentgenograms taken 1 and 5 years after operation are shown, and this joint today presents about 80 degrees' voluntary flexion from complete extension. There appears to have developed a definite joint space.

This was the first case in which the procedure was employed and permits a comparison over a 5 year period of two different methods of treatment.

CASE 2. P. Z. (Figs. 3, A and B). A girl of 4½ years was admitted to the Hospital for the Ruptured and Crippled in November, 1932, presenting a congenital dislocation of the right hip. This patient had never had any previous treatment for the dislocation and presented the characteristic findings of a unilateral dislocation. There was a half inch shortening and a positive Trendelenburg.

November 21, 1932, first stage.

December 5, 1932, the second stage.

At present the child walks without a limp. There is no shortening and she has a normal range of movement. Attention is called to the width of the joint space and the size and apparent smoothness of outline of the epiphysis 3½ years after operation.

CASE 3. A. Y. (Figs. 4, A, B, and C). A girl of 6 was admitted to the Orthopedic Service of Bellevue Hospital in April, 1933, presenting a congenital dislocation of the right hip. When the child was an infant several attempts had been made to reduce the dislocation but none had been successful. The child was in good general condition and presented the characteristic gait of a right-sided dislocation. Trendelenburg test was positive and there was shortening of three-quarters of an inch.

April 20, 1933, the first stage.

A B

Fig. 6. Case 5, D. R., girl of 3 years presenting congenital dislocation of the right hip with some instability of the left. B, 13 months after operation. Shows secure right hip with excellent range of movement in all directions. Left hip not treated.

May 5, 1933, the second stage.

At present the child walks without a perceptible limp. There is no shortening, and she presents an almost normal range of movement in all directions. Roentgenograms 2 years after operation show a well formed joint space, and the epiphysis is smooth in outline and appears to be developing normally.

CASE 4. D. K. (Figs. 5, A and B). A girl of 4½ was admitted to the Hospital for the Ruptured and Crippled in December, 1933, presenting a congenital dislocation of the left hip. This child had previously had three attempts at closed reduction and each time the dislocation had recurred on removal of the plaster. The child was in good general condition and presented a marked limp on walking. There was half an inch shortening.

January 3, 1934, the first stage.

January 15, 1934, the second stage.

At present the child walks without a perceptible limp. There is no shortening and she presents a normal range of movement. Roentgenograms before operation and 2 years after operation are shown.

CASE 5. D. R. (Figs. 6, A, and B). A girl of 3 was seen at the Hospital for the Ruptured and Crippled in January, 1935. This patient had been under treatment at this hospital for the previous 6 months where the right congenital dislocation was reduced by closed manipulation but had redislocated. The child presented a rather insecure left hip and a frankly dislocated right hip. There was the characteristic limp on the right on walking and a shortening of ½ an inch.

No preliminary traction was necessary in this case.

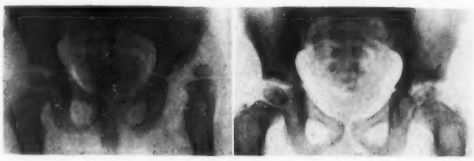
February 13, 1935. Second stage on right hip.

At present the child presents no shortening and no Trendelenburg on either side. She is very active and has a good range of movement of the right hip in all directions. Roentgenograms before operation and 1 year after operation are shown.

CASE 6. B. A. (Figs. 7, A and B). A girl of 3 years and 10 months was admitted to the Hospital for the Ruptured and Crippled in October, 1935. This child had previously had two unsuccessful attempts at closed reduction. She presented a right congenital dislocation with a shallow acetabulum with a deficient roof, so that further attempts at closed reduction were not considered. She was in good general condition and presented the characteristic limp on walking.

October 1, 1935, the first stage.

October 25, 1935, the second stage.



A B

Fig. 7. Case 6, B. A., girl of 3 years and 10 months presenting a right congenital dislocation. B, One year after operation. Has an increasing range of movement in all directions and walks without a limp.

At present the child is walking with a barely perceptible limp. She shows no shortening and has a range of movement from 180 to 80 degrees with a slight limitation of movement in all other directions. Roentgenograms before and 1 year after operation are shown.

SUMMARY

1. A two stage operative procedure for congenital dislocation of the hip is presented. It represents an attempt to devise a procedure in which not only actual reduction and stability can be promised but by preserving the synovial and capsular covering about the head, an opportunity is afforded for obtaining a free range of movement.

2. The preliminary lengthening of the contracted tissues by the first stage described is felt to be a very essential step.

3. If the capsule covered head does not slip easily into the reamed out acetabulum and requires any forcible reduction, pressure necrosis of the synovial cells may occur, limiting the opportunity for future motion.

4. It is felt that this procedure is best suited to patients under the age of 10 years.

5. Sufficient time has not elapsed for an end-result study to be made of this procedure, but the method is presented in the hope that it may be tried by others and properly evaluated.

FRACTURES OF THE OS CALCIS

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THE longitudinal arch of the foot has for its posterior base the os calcis, and for its anterior base, the heads of the metatarsal bones. On the inner side, the highest point of the arch is at the junction of the astragalus and scaphoid, and on the outer side it is at the calcaneocuboid juncture. The latter point is at a considerably lower level than the former, and this arrangement forms a semidome. The foot will tolerate a gradual lowering of this arch fairly well, but any sudden lowering, as a result of trauma, is always attended with distressing symptoms. Fracture of the os calcis may lead to such an abrupt lowering of the arch, and to such an alteration in the semidome shape that great disability will ensue.

STATISTICS BASED ON FIFTY-FOUR CASES AT THE CLINIC

In a consideration of any fracture, it is usual to present a classification embracing the various types of fractures encountered in the bone under discussion. This I am not going to do because it has been well done in the textbooks on fractures, and such a presentation would consume so much time that it would be impossible to consider the clinical phases of this troublesome fracture. I will not attempt to give any estimate of the average length of disability, for, after a careful review of the clinical records of 54 consecutive cases of fracture of the os calcis in the files of The Mayo Clinic, I was so much at sea that I realized the futility of such an attempt. So many factors enter into such an estimation that such a study is of no practical value.

The study of these records, although disappointing from the viewpoint mentioned, nevertheless furnished some information of interest. In the 22 cases in which there were fresh fractures, 20 of the patients were males and 2 were females. In 3 of these cases there were double fractures. Seventeen of the fractures were the result of falls; 2 of the fractures, which were double, were the result of explosions from below, which had forced the floor upward; 1 was the result of an automobile accident, and in 2 instances the type of injury was not recorded. Three of the fractures were compound. In 6 cases the results were not known. In 7 cases the results were excellent, and the patients returned to full duty, usually in 3 to 4 months, with little pain. In 6 cases, in which the results were classified as good, the patients were able to carry on, but with some pain and discomfort. In 2 cases the results were only fair, but at the end of a year the patients were able to get about and carry on their activities; one of these patients was a farmer and the other was a housewife. One patient, a railroad employee, who was 67 years of age, claimed that he was completely disabled, 2 years after the accident.

These results are much better than one would be led to expect, according to the literature. Why is this? It is not because of any specific type of treatment, for the majority of these patients were treated with plaster-of-paris casts, which were applied after a molding of the fragments was done in an effort at reduction. The reason is that the length of time is not taken into consideration and comparatively few were industrial compensation cases. As long as 6 years have elapsed in some cases since the accident and, although the result would have been classed as fair, or perhaps poor, when the patients first resumed work, gradual improvement has taken place. In the tabulation of the results, no consideration is given to the anatomical restoration; only function is considered. The return to duty was delayed in those cases in which the patients received compensation insurance, and improvement took place more slowly in those cases in which no job was awaiting the patients than it did in cases in which a job was available. The occupations of the patients varied: 2 were farmers, 2 were painters, 1 was a plasterer, 3 were carpenters, and 5 were laborers. Eleven of the 22 were more than 50 years of age.

To evaluate figures of this kind properly, many factors would have to be considered, such as the type of fracture, associated injuries, and so forth. To deal further with statistics is useless, but I would like to mention briefly the 32 patients who came to the clinic because of old fractures of the os calcis. In these cases the length of time which had elapsed between the occurrence of the fracture and the arrival of the patient at the clinic varied from 12 weeks to 26 years. None of these patients had been treated at the clinic primarily. Five were more than 50, 14 were between 40 and 50, 9 were between 30 and 40, and 4 were between 20 and 30 years of age. There were no women in this group.

The cause of the disability in 21 cases was definitely recorded as astragalocalcaneal traumatic arthritis. Arthrodesis was advised in 14 cases, but only 3 patients were operated on. The reasons that so few accepted the advice are several. First, the disability was of long duration and the patients could get about. Second, there was the dread of the complete disability, which would last for 3 months and perhaps longer if arthrodesis were done, and the consequent loss of earning power and expenses incidental to the procedure. Third, most of the patients felt that they were slowly improving and that, by aid of the proper shoes and reasonable care in walking, they would be able to reduce their discomfort.

LENGTH OF DISABILITY

It may be assumed safely that compensation insurance has definitely prolonged the disability which follows fractures of the os calcis, and, therefore, this fracture perhaps has received a blacker name than it deserves. When the individual can receive as much for doing nothing as he can for doing what he is able to do, there is no incentive for him to return to work, for he can only do part time work when he first returns, and his earnings under those conditions will be small. This situation prompted Conn, of Akron, to advance his admittedly complicated program to shorten the disability. He advised immediate manipulation and skeletal traction, to be followed 5 weeks later by astragalocalcaneal, astragaloscaphoid, and calcaneocuboid fusion. In cases of old fractures, he advised the triple fusion alone.

PATHOLOGY AND TREATMENT

The pathological changes in fractures of the os calcis vary with the force and its line of transmission. Boehler has studied the type of fractures encountered in a large series of cases and has tabulated eight types. I will make no attempt to discuss these. The fractures which cause the greatest trouble are those of the "crunching" type, in which there are varying degrees of damage to the articular surfaces and to the sustentaculum tali. The latter is fractured much more often than is generally supposed although isolated fractures of this process are rare. It often has been said that if the astragalocalcaneal joint is not broken into there will be no subsequent arthritis in that joint. Such a statement is not correct. The fracture through the body, which often is associated with upward displacement of the posterior portion, leads to such changes in the form of the os calcis that the weight-bearing lines are more or less altered, and the normal articular surfaces of

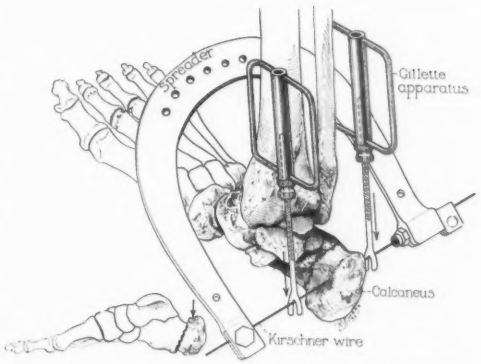

Fig. 1. Insertion of Kirschner wire and use of the Kirschner stirrup and push rods.

the astragalus and the calcaneus bear the weight through greatly altered planes. Boehler's interesting observations on the salient angles have demonstrated this fact. Definite traumatic arthritis ensues, with thinning of the articular cartilage and formation of adhesions.

The aim in reduction should be restoration of the fragments of the fractured bone to their normal relationship. This is not easily secured in most cases, for a fracture of the os calcis is often produced by great force and there is comminution with a certain amount of irreparable crunching of the lamellæ of the substantia spongiosa. The fracture may be almost stellate and fragments may be multiple. All that can be done then is the molding which has been advocated and carried out so skillfully by Boehler. In other more fortunate instances, the posterior tubercle may be merely pushed upward, and there may be little crunching of the substantia spongiosa. It not only is difficult to reduce it, but also to make it stay in position. Various methods have been advocated and one, which was advised by Gillette, I have used with some degree of success in several instances. I think the Kirschner wire could be used to advantage over the rather heavy peg or nail advocated by Gillette.[1] By incorporating a pair of crutch-like pushers that fit over the wire or peg, and by inserting the threaded arm of the crutch, on which is a set-screw, into metal canals incorporated in the cast, pressure can be made downward on the wire, and thus on the displaced fragment (Fig. 1). The wire or peg must be accurately placed in the displaced fragment to insure its reduction. If placed too far forward, it

[1] A personal communication from E. P. Gillette, Toledo, Ohio, states that he has modified his original technique by putting a pin through the tibia, incorporating it in a cast. He is thus able to leave the knee free.

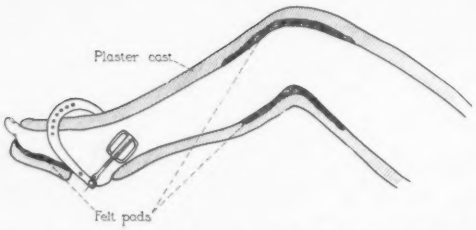

Fig. 2. Leg in cast with knee flexed and Kirschner wire through os calcis.

does little good for it leaves the tubercle tilted upward by the tendo achillis. By flexing the knee to a right angle, thus relaxing the tendo achillis, and padding well the popliteal space and the knee, particularly anteriorly, great force can be put on the fragment by this arrangement (Fig. 2).

Conn, by aid of an ingenious instrument, inserted slotted metal strips on each side, into the transfixing pins in the tibia and os calcis, and incorporated them in plaster.

These procedures are, on the whole, too complicated for the surgeon, with no special equipment, and are rarely used. The majority of fractures of the os calcis will continue to be treated in the old way, by manipulation and casts. By such means, very little reduction of the fragments actually is accomplished. Late poor results, therefore, will demand interference, but the majority of patients, after varying periods of disability, will attain such a degree of functional improvement that they may resume their duties although they may be handicapped to a degree.

RECONSTRUCTION IN OLD FRACTURES

There are three relatively common sequelæ that can be remedied to a certain extent by operation. First, in fractures in which the posterior portion of the os calcis is shoved upward and allowed to unite in that position, a protuberance or exostosis may form on the inferior surface. Chiselling this away and smoothing down the surface does help. The arch may be very definitely flattened, but the foot will gradually accommodate itself.

Second, beneath the external malleolus, where the external supporting wall of the bone gives way, along the region of the peroneal groove, a callus may form that almost impinges on the malleolus when the patient walks. Chiselling this away will relieve the patient of much of the pain.

Third, the distortion of the os calcis and altered weight-bearing lines may distort the articulation of the astragalus and scaphoid and that of the os calcis and the cuboid sufficiently to produce very definite traumatic arthritis in these joints so that, even though the chief fault lies in the astragalocalcaneal joint, fusion of this joint alone will not relieve the patient. In addition, the two other joints mentioned should be fused, and the typical triple arthrodesis, which has been found so useful in the treatment of flail feet following infantile paralysis should be carried out. Although lateral mobility, which is permitted by the astragalocalcaneal joint, will be destroyed, these patients already have but little of it left, and what is left is only a cause of discomfort. Furthermore, the varying degrees of compensatory movement of the forefoot soon develop and help to compensate for the rigidity of the posterior portion of the arch.

CONCLUSIONS

1. Fractures of the os calcis leave in their wake considerable disability that over a term of years gradually lessens until most patients are able to resume their occupations.

2. The length of time that the discomfort persists, and the inability of the patient to carry on full duty, place these fractures as a particularly bad group for compensation insurance and explain the wherefore of the advancement of such an admittedly complicated program as that of Conn.

3. The majority of fractures of the os calcis will be treated by less complicated procedures. In cases in which disability persists as a result of exostosis or traumatic arthritis, the patients can be treated advantageously by removal of the exostosis and by triple arthrodesis of the astragalocalcaneal, astragaloscaphoid, and calcaneocuboid joints.

BIBLIOGRAPHY

1. Boehler, Lorenz. Treatment of Fractures. Pp. 460–485. Baltimore: William Wood & Co., 1935.
2. Conn, H. R. The treatment of fractures of the os calcis. J. Bone & Joint Surg., 1935, 17:392–405.
3. Gillette, E. P. An apparatus for treatment of fractures of the os calcis. J. Bone & Joint Surg., 1930, 28:670–671.

THE BLADDER COMPLICATIONS OF CARCINOMA OF THE CERVIX[1]

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A GENEROUS experience with the urological complications of carcinoma of the cervix and an opportunity to study the records of 683 cases of this condition, have led to the conviction that too little attention has been directed to the fact that the spread of this disease commonly affects the organs of the urinary system. In another communication about to be published, we have discussed the high incidence of ureteral occlusion and have shown, in a large series, that significant obstruction of the ureters occurred in 78 per cent of those patients in whom there had been malignant invasion in the regions of the broad ligaments. In this paper, it is our purpose to consider separately the changes which take place in the urinary bladder in cervix carcinoma as a direct result of the disease, or during the course of its treatment.

Our material is drawn from the 683 cases of cancer of the cervix that have been admitted to the Pondville Hospital (Massachusetts Department of Public Health), since its establishment in June, 1927, and until January, 1936. These have been reviewed through the courtesy of Dr. J. V. Meigs, chief of our department of gynecology. From this group we have selected 209 cases in which the clinical evidence pertaining to the bladder was sufficiently complete to serve as a basis for this discussion.

The ages of these patients were as follows: 21 to 29 years, 5 cases; 30 to 39 years, 37 cases; 40 to 49 years, 68 cases; 50 to 59 years, 48 cases; 60 to 69 years, 34 cases; 70 to 79 years, 17 cases. The American College of Surgeons classification was used in denoting the extent of disease. There were in Class A, 10 cases; Class B, 18 cases; Class C, 67 cases; and in Class D, 114 cases. Grouping as regards degree of malignancy of the cervix tumor was based upon three grades, of which Grade 1 represents the adult, well differentiated epidermoid carcinoma, and Grade 3, the highly malignant, undifferentiated type. The report was Grade 1, in 22 cases; Grade 2, in 53 cases; and Grade 3, in 60 cases. There were 59 reports of epidermoid carcinoma, ungraded; in practically all of these, previous radiation therapy before admission at Pondville precluded the possibility of more accurate histological description. Thirteen cases were classified as adenocarcinoma, and in 2 instances the exact type of tumor was unknown. As regards the character of growth, three general types are recognized; proliferative, ulcerative, and invertive. The proliferative group includes those cases in which growth is chiefly outward from the cervix. These tumors are described commonly as fungating, outcropping or cauliflower-like in form. Vaginal extension, mucosal or submucosal, may occur in this group. The ulcerative type leads to the destruction of the cervix, but may extend also along the walls of the vagina. The invertive or infiltrative tumors are predominantly endocervical. All three types, of course, may extend upward and laterally into the broad ligaments, posteriorly toward the rectum, or anteriorly toward the bladder.

Seventy-four of the series are living, and 135 have died. There were 93 autopsies. One hundred and six of the 209 patients under consideration received their first treatment for malignant disease of the cervix at the Pondville Hospital. Twelve were untreated cases, and the remainder had had treatment in other institutions before entering Pondville. Practically all of the latter group were given further therapy with roentgen-ray or radium after admission.

Natural variation in the thoroughness of history-taking, and the common occurrence of bladder disturbances in women not afflicted with cancer, make it futile in this discussion to attempt an analysis of clinical symptoms, or to derive fixed conclusions from such complaints when present. In some instances there appear to be no significant symptoms; many report an increased frequency of urination, and it is our impression that this is the most common of the symptoms referable to the bladder. Painful micturition, which may result from the advent of infection or extravesical pressure, or actual malignant invasion of the bladder, was reported by some of the group. As regards hematuria, the clinical history is often inaccurate and unreliable, in carcinoma of the cervix. Four of the 12 cases in our series who had radium ulcerations of the bladder proved by cystoscopy, gave a record of the sudden appearance of blood stained urine. Hematuria in some degree, either gross or microscopic, must occur much more frequently than the records would indicate in all those cases in which there

[1]Read before the Philadelphia Urological Society of the American Urological Association, Philadelphia, Pennsylvania, March 23, 1936.
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TABLE I.—NEGATIVE CYSTOSCOPIES

	Class				Grade					Type of disease			
	A	B	C	D	1	2	3	AC	E	P	U	I	?
Before treatment (10 cases)	1	2	6	1	1	4	4	0	1	5	3	2	0
After treatment (6 cases)	2	1	2	1	0	0	1	5	0	1	2	2	1
Total—16	3	3	8	2	1	4	5	5	1	6	5	4	1

P—Proliferative.
U—Ulcerative.
I—Infiltrative or inverting
?—Unknown at outset
AC—Adenocarcinoma
E—Epidermoid carcinoma, ungraded

TABLE II.—CYSTOSCOPIC FINDINGS

		Class				Grade					Type of disease			
		A	B	C	D	1	2	3	AC	E	P	U	I	?
Primary cases Before treatment (22 cases)	EVP	0	0	6	2	1	2	4	1	0	3	1	4	0
	TE	0	0	3	1	0	0	2	1	1	1	1	0	2
	EVP & TE	0	1	4	5	2	1	5	1	1	7	3	0	0
During treatment (18 cases)	EVP	0	2	4	1	2	2	3	0	0	3	2	1	0
	TE	0	0	1	0	0	1	0	0	0	0	0	1	0
	EVP & TE	0	2	8	0	1	3	3	3	0	6	3	1	1
Secondary cases After treatment elsewhere (13 cases)	EVP	0	0	2	1	1	0	0	1	1	1	0	0	1
	TE	0	0	2	5	0	1	0	0	3	2	0	0	5
	EVP & TE	0	0	2	1	0	0	2	0	4	2	0	1	1
Total—53		0	5	32	16	7	10	19	7	10	25	10	8	10

TE—Trigonal edema
EVP—Extravesical pressure

has been mucosal involvement by radium reaction or by tumor.

The story of incontinence is equally difficult to evaluate. Next to increased frequency, we found it the most common symptom. Except perhaps in cases of large vesicovaginal fistulas, it is partial rather than complete. Obviously the presence of a profuse discharge from the vagina may lead to uncertainty on the part of the patient as to the actual existence of urinary leakage. It is our opinion that loss of control when present, results chiefly from extravesical pressure and distortion in the region of the bladder neck, or from a vaginal fistula, more often than from any of the other causes which might be predicated in this condition, such as malignant invasion of the vesical outlet, or the effect of massive irradiation.

Partial retention with residual urine may occur in some of these cases, but we have no definite information concerning it. Complete retention due to urethral obstruction by tumor has been encountered in a few instances in this series.

There were in this series 105 patients who were examined by cystoscopy on one or more occasions. Forty-three were so studied prior to direct cervix therapy which, in this as in the whole group, consisted usually of radium application, or high-voltage roentgen-ray, or both. Sixty-two were examined for the first time, during or after treatment. In 16 of 105 cases, there were no noteworthy changes to be seen within the bladder; in 10 of these the cystoscopic examination was made before cervix therapy was begun. For further data concerning this negative group, see Table I.

Many patients showed at cystoscopy the earliest sign of direct bladder disturbance by the malignant process, in the form of distortion from extra-vesical pressure (Table II). This consists usually of a uniform elevation of the proximal trigone and posterior wall, covered with normal mucosa and unaffected by distention. It may resemble the ordinary uterine eminence seen so often in the female bladder floor, or may be so accentuated as to form deep lateral sulci on each side. Obviously the distortion must be interpreted with care and must be correlated always with the findings on pelvic examination. It may be produced by the tumor, or by the reaction following radiation; by an inflammatory process in or around the uterus, or merely by an anterior-lying fundus.

TABLE III.—TUMOR BY CYSTOSCOPY

	Class				Grade					Type of disease			
	A	B	C	D	1	2	3	AC	E	P	U	I	?
Before treatment Primary cases—7	0	2	1	4	0	1	4	0	2	3	3	1	0
During treatment Primary cases—8	0	0	5	3	0	0	7	0	1	5	1	2	0
After treatment Secondary cases—8	0	0	2	6	0	2	1	0	5	0	5	0	3
Total—23	0	2	8	13	0	3	12	0	8	8	9	3	3

Extravesical pressure has been referred to by many writers. Marzetti calls it *bombement* and states that it is the most common abnormality found by cystoscopy in carcinoma of the cervix. It is of interest that Korkhov found by cystoscopic inspection, definite improvement in the bladder outline in 50 of 100 cases following radiation therapy. Aman-Jean reported similar observations and believed that cystoscopy might serve as a guide to the efficacy of treatment, by revealing the presence or absence of such change. We are quite in accord with these conclusions.

As malignant disease advances toward the bladder, or comes actually to invade it, one sees localized areas of congestion and submucous hemorrhage followed still later by edema. Edema, usually associated with distortion by extravesical pressure, was observed frequently (Table II). It probably signifies in most instances the presence of carcinoma in the bladder wall beneath the edematous area as Schmitz, Vermooten, and others have agreed. However, one might suggest the occasional possibility that inflammatory reaction around the tumor in a region adjacent to the bladder might produce a similar picture. The edema resulting from radium reaction will be discussed in a later section.

Further invasion of the bladder by tumor may lead to submucous nodules or definite neoplasm projecting into the vesical cavity, with or without ulceration (Table III). Actual tumor was apparent at the time of cystoscopy in 23 cases of this series; 15 of them presented such evidence before or during cervix treatment. In the remainder these changes were observed some time after the completion of active therapy. Herger and Schreiner, in a clinical study of 50 cases of advanced carcinoma of the cervix, found 14 instances of ulceration and infiltration of the vesical mucosa. Faerber reported bladder involvement in 58.7 per cent of 150 postmortem examinations.

It is of interest in this regard, that cystoscopy may lead to more accurate classification of the case than is possible without bladder inspection. For example, 10 of our 23 cases with definite intravesical involvement had been classified as B or C cases on pelvic examination, but the proof of extension into the bladder places them at once in the D group. Furthermore, this would indicate that extension from malignant disease of the cervix sometimes may involve the urinary bladder before palpable invasion of the broad ligaments has occurred.

The end-stage of this whole process of malignant invasion, as far as the bladder is concerned, lies in the formation of a vesicovaginal fistula. Indeed, it is possible that most patients with actively progressive disease will develop this condition unless death occurs sooner from some other complication, such as hemorrhage, or uremia due to ureteral occlusion. We have found definite records of vesicovaginal fistulas in 62 of 683 cases of carcinoma of the cervix at the Pondville Hospital (Table IV). Of this large series, 226 are living, and 199 died at Pondville. We have, therefore, dependable information concerning 425 patients. In this number there were 55 known fistulas (12.9 per cent). The incidence among those who died in the hospital was 24.4 per cent; we know of 7 cases among those 258 who died

TABLE IV.—VESICOVAGINAL FISTULAS—62 CASES

Class	No.
A	2
B	3
C	11
D	46
Grade	
1	3
2	19
3	16
AC	0
E	24
Type of Disease	
P	12
U	37
I	3
?	10

TABLE VA.—NECROPSY FINDINGS

	Class				Grade					Type of disease				
	A	B	C	D	1	2	3	AC	E	P	U	I	?	%
Negative (28 cases)	1	1	3	23	3	9	5	3	8	10	8	1	9	30.1
Wall invasion (12 cases)	0	0	4	8	1	4	4	1	2	4	6	1	1	12.9
Mucosal invasion (22 cases)	0	1	7	14	4	5	7	3	3	9	8	1	4	23.7
VV fistula (31 cases)	0	2	4	25	3	13	8	0	7	3	17	0	11	33.3
Total—93	1	4	18	70	11	31	24	7	20	26	39	3	25	

outside the hospital, but if all the facts were available in this group, the incidence probably would be comparable. In the list of 226 living patients, there are 7 with fistulas. Many of this living group are cured, but the incidence of fistula will increase, of course, among those who still have progressive disease. When active disease is present, it is our feeling that the development of fistula may be accepted as a bad prognostic sign, since the average length of life in our fistula group was but 0.4 years (about 5 months) after the appearance of this complication.

In its earliest stages the vesicovaginal fistula may be so small that its clinical or even its cystoscopic recognition will be difficult. This accounts, doubtless, for the fact that the highest incidence, 33.3 per cent, was found in our postmortem group of 93 cases. At autopsy, minute communication between the bladder and vagina may be detected, large enough only for the passage of a probe. It is true also that fistulas occurred more frequently among those patients who had further therapy at Pondville, after having had treatment in other institutions before admission. It is possible that such secondary cases may have, as a rule, more advanced malignant disease; it is probable also that the effects of retreatment play an important part. We had 20 cases of fistulas in our primary therapy group (4.7 per cent), while there were 42 fistulas (16.3 per cent) in the group which had had treatment elsewhere before coming to Pondville. Not all of the latter group were re-treated in our clinic, but re-treatments, especially with radium, were more frequent in these secondary cases than in those in which the initial therapy had been given at Pondville. There were 7 patients who developed vesicovaginal fistulas before treatment of any kind had been given; it is interesting that one of these now shows no evidence of active disease, 2½ years after treatment, but the fistula remains. Of the whole series of 62 cases with fistula, 7 showed complete regression of malignant disease; 3 of these have died, and while the postmortem examinations showed ureteral occlusion, carcinoma was not found.

TABLE VB.—NECROPSY FINDINGS

	Cases
Negative	12
Bladder alone	13
Ureters alone	16
Ureters and bladder	52
Total	93

Showing frequency of bladder and ureteral involvement.

As has been stated, there were 93 cases studied at autopsy (Tables VA and VB). It will be noted that 69.9 per cent presented bladder involvement varying in degree from invasion of the wall, to vesicovaginal fistula. Behney has reported an impressive series of 166 postmortem examinations in cases of advanced carcinoma of the cervix, in which he found an incidence of fistula between the bladder and vagina of 22.3 per cent. In 86 of his series there had been no treatment, and 25.6 per cent of this group had fistulas. The incidence in the treated cases was 18.7 per cent. He did not comment upon the lesser degrees of bladder involvement. Warren, in another autopsy study, reviewed 102 cases of malignant disease of the cervix and found that there were fistulas in 36 patients (35.3 per cent). He did not find a significant difference in incidence between the treated and untreated groups. Williams reported fistulas in 38 per cent of the untreated cases in a large postmortem series. Faerber found fistulas in 45.3 per cent of his cases.

The facts presented in Table VB are informing concerning the pathway of extension from carcinoma of the cervix and demonstrate that the local spread of disease may be anterior toward the bladder before marked parametrial involvement has occurred. We have seen patients clinically classified as B cases, without broad ligament

TABLE VI.—RADIATION REACTION

	Class				Grade					Type of disease			
	A	B	C	D	1	2	3	AC	E	P	U	I	?
Primary (8 cases)	4	2	2	0	2	2	2	0	2	3	1	4	0
Secondary (4 cases)	0	1	3	0	0	0	0	0	4	0	0	2	2
Total—12	4	3	5	0	2	2	2	0	6	3	1	6	2

extension—who were found at cystoscopy to show intravesical invasion. On the other hand, the bladder may appear normal in the presence of broad ligament involvement sufficient to result in ureteral occlusion.

Among our 93 postmortem studies there were 10 patients who had had no treatment directed to their malignant disease. Seventy per cent of them had some degree of bladder involvement; one showed invasion of the vesical wall; in 3 there was extension into the mucosa, and 3 had vesicovaginal fistulas. Although this group is small, it will be seen that these figures closely parallel those already presented for the entire series.

A very interesting and important phase of this entire subject of bladder complications in carcinoma of the cervix, is presented by a condition which results from the treatment of this disease rather than from the disease itself. We refer to the remote radium reaction, a lesion unrecognized until relatively recently, and one which, until better understood, gave rise to considerable diagnostic confusion in these cases. The earliest descriptions were written by Haendly, Schugt, Zeiss, Kahn, and Dean, and more recent discussions of the subject have been published by Ottow, Smith, Colby, and others.

In general, it may be stated that there are two types of radiation reaction within the bladder. First there may be the early or acute reaction which occurs at the height of the radiation effect in the cervix itself. This is comparable to the mucosal changes seen often in the buccal cavity following external irradiation for malignant disease. The reaction in the bladder which may vary in degree, gives rise to the symptoms of cystitis that patients report so frequently soon after treatment. It is true, doubtless, as Ottow has said, that this acute process may subside or may advance to actual ulceration and even fistula as occurred in one case in our series.

The late or remote radiation reaction in the bladder is the more definite clinical entity and the one usually referred to in discussions of this subject. It is analogous to the skin changes with which we are all familiar and to the radionecrosis that occurs sometimes, in tissues elsewhere in the body following massive irradiation. It results primarily from vascular changes which may vary in degree from mild transient interference with local blood supply, to complete obliterative endarteritis with ischemic necrosis. The lesion produced in the bladder, therefore, will depend upon the extent of these effects. Cystoscopic examination may find nothing more than a circumscribed area of hyperemia and edema, or there may be a zone of complete devitalization with ulceration and slough. The ultimate fate of the region involved will depend upon the depth of injury, and this may not be determined usually by a single cystoscopic inspection. It is probable that there is eventual healing in the greater number of cases, and that when healing occurs the mucosal and submucosal layers have been chiefly affected. It is reasonable that the minute arterioles, venules, and capillaries that supply these inner layers should be more susceptible to injury and more vulnerable to obliterative changes than the larger vessels nearer the bladder periphery. When, however, these larger vessels are involved in this process, the depth of necrosis in the vesical wall may be so great as to preclude the possibility of local recovery, and lead even to fistula.

In our series, there were 12 cases of late radiation reaction in the bladder (Table VI). The average length of time from the first radium treatment to the onset of bladder symptoms was 2.25 years. The shortest interval was 0.7 years, and the longest, 5.5 years. It is interesting and probably significant that three patients in this group had re-treatment with radium some time after the initial dose, and that for them the average time before the development of the vesical lesion was 1.1 years after the last treatment; the shortest interval was 0.5 years, and the longest, 1.5 years.

The symptoms, in our experience, consist chiefly of dysuria, hematuria, and increased frequency of micturition, usually of relatively acute onset. Such symptoms, reported long after the

treatment of the cervix and in patients free from local disease, are highly suggestive of the presence of radiation reaction within the bladder.

The conditions found by cystoscopy will vary as we have stated. The most common picture is that of a central, sharply defined area of slough surrounded by a zone of hyperemia and edema. The edema may present as minute blebs, or raised reddened ridges. Obviously, the radiation reaction will occur in the region of greatest radiation effect, and its location in the bladder, therefore, need not be the same in all cases. The most frequent site, as we have found it, is in the posterior midline just above the trigone. The common involvement of this region is due in large measure probably, to its anatomical location with reference to the cervix. We would suggest, however, that there may be another influence in the possibility of a less rich vascularity in the midline of an organ deriving its blood supply from main vessels which enter it laterally on each side.

Clinical differentiation between a late radiation reaction within the bladder and invasion by tumor is sometimes difficult, and especially so when the lesion is first observed. Repeated examinations with reference to progression or regression usually are helpful, but the decision cannot be made, often, by the cystoscopic picture alone. A history of radium treatment of the cervix followed by a prolonged interval of many months or even years before the appearance of the lesion in question weighs heavily in favor of the radiation reaction. The presence or absence of active disease in the pelvis cannot determine the diagnosis, but freedom from palpable tumor argues of course against malignant invasion of the bladder. We have observed in some instances of radiation reaction, that thickening, perhaps edema, and tenderness may be felt in the anterior vaginal wall opposite the area involved. In general, it is our impression also, that the urinary symptoms produced by late radium effect are more insistent and more acute than those arising from early invasion by tumor, and that such symptoms when so produced, usually subside quite satisfactorily with simple measures of local treatment, continued until inspection with the cystoscope finds that healing is complete. Removal of tissue for biopsy may be resorted to but we do not believe that this should be necessary in most cases and we do not recommend it.

EVALUATION OF STUDY

There are certain general impressions to be derived from the foregoing text and tables, which undoubtedly have much bearing on the involvement of the bladder from carcinoma of the cervix and its treatment. It is quite obvious and well known, that the more advanced the local disease, the greater the likelihood of vesical invasion. It can be seen from perusal of the tables that the proportion of the early to the advanced cases in the group with negative cystoscopic findings is much greater than in the positive groups where the moderately advanced and advanced cases are overwhelmingly in the majority. The extent of disease, therefore, should offer a reasonable indication as to whether or not the bladder is involved. Generally speaking, this may be true, but as has been stressed before, it is exceedingly difficult to determine the extent of disease by pelvic examination alone. For instance, as has been emphasized by others, a case which clinically presents evidence of broad ligament extension may have nothing more than carcinoma confined to the cervix and immediate paracervical region, with an inflammatory process accounting for the lateral involvement. In contrast with this is the patient who on vaginal and rectal palpation does not reveal any parametrial change, but in whom inspection of the bladder shows either suggestive or definite invasion of this organ by tumor, thereby altering at once the original clinical concept. There is further confirmation in our postmortem series, which, as has been stated previously, shows that the mode of dissemination of the disease varies considerably and may involve the bladder without any evidence of broad ligament extension. The reverse of course is also true. Cystoscopic examination, therefore, may be just as important as pelvic and pathological examinations in determining the true status of the case in question.

The relationship between the grade of carcinoma and intravesical invasion is difficult to evaluate, since a single biopsy, especially a superficial one, does not always reveal the relative malignancy of the tumor. In general, it may be said that the highly malignant neoplasms are more likely to extend into the bladder.

We would like to advance at this time, the importance of the clinical type of tumor with respect to vesical invasion. If one considers the position of the cervix in relation to the bladder, it can be seen that the liability to bladder involvement by tumor varies definitely with the nature of the growth. The proliferative type, which is not infrequently of a lower grade of malignancy, because of its bulky character is likely to produce at cystoscopy the picture of extra-vesical pressure (Table II). Some tumors of this type extend into the bladder, but submucous infiltration of the

vagina usually precedes this extension. When intracervical radium is used in this kind of lesion, the bulk of the tumor gives added protection to the bladder so that severe radiation reactions seldom occur. If radium seeds are introduced, such reaction when it does occur, depends entirely upon the proximity of the bladder to the site of the application.

The ulcerative type of growth is usually of higher malignancy and seems to possess a greater tendency to vesical invasion than the others. This can be easily understood when the character of its behavior is considered. It is distinctly destructive, and once the cervix is even partially destroyed, continuation into the bladder may follow more easily, producing in sequence, intramural and mucosal invasion, and finally fistula. This is illustrated by the frequency of this type of lesion in the untreated cases which show a high percentage of bladder involvement. It is in this type also that fistula may result from the application of radium, since the vesicovaginal septum is considerably thinned bringing the bladder closer to the site of radiation. It is possible also that in cases of actual vesical involvement by a radiosensitive tumor, regression may occur so rapidly under treatment as to preclude the possibility of healing and so produce a fistulous communication with the vagina. It has been contended by some that radiation is the major factor in the production of fistulas. We recognize its importance but we agree with Cutler, Smith, and others, that the vesicovaginal fistula in carcinoma of the cervix, is usually a manifestation of progressive disease. The incidence in our living group is low, a fact which lends further evidence in addition to our postmortem statistics, that advancing disease is the predominant influence in fistula formation. Fistulas may be produced by radium, but as is stated by Cutler, the cause may lie not so much in the radium itself, as in faulty technique of application, with failure to keep applicators in proper position, or lack of sufficient packing against the bladder. Other factors of importance are inadequate filtration, excessive doses, and re-treatment with radium in an area which has had already irradiation to the limit of local tolerance.

The invertive or endocervical type seldom grows toward the bladder, but here too one may see evidence of tumor by cystoscopy or at autopsy (See Tables III and VB). This form of tumor is characteristically infiltrative and may remain confined to the cervix for a relatively long time before extending into neighboring structures. As will be seen by Table VI, this type predominates in the cases with radiation reaction within the bladder. The intervening tissue offers greater protection than in the ulcerative form, but less than in the proliferative type of growth. The vesical changes due to radiation are usually late and seldom progress to fistula.

In every instance of late radium reaction in the bladder in our series, radium seeds—occasionally glass but usually gold—were used in the treatment of the cervix. (Intracervical silver applicators were used in conjunction with the seeds in some cases.) We believe this to be of great significance, since inadequate filtration and the site of insertion in the periphery of the growth, undoubtedly play the greatest part in the production of this sequela. It seems significant in this connection that we have observed no radiation reactions in those cases in which treatment has been given at Pondville since early in 1931. This corresponds with the time of the discontinuance of the use of gold seeds as a routine measure. Seeds are now employed only in the treatment of small areas of recurrence in the cervix or vaginal wall. An additional obvious factor in the problem may be the use of massive or excessive dosage.

Another group to be considered is that in which fistula developed in cases without disease, a considerable time after treatment. Our series includes 6 such cases, and the average lapse of time between the first treatment and the appearance of the fistula was 4 years. Two interpretations may be offered. First, the fistula may be the final manifestation of a radio-necrosis which could not heal because of irreparable damage to the blood supply in the bladder wall and vagina. This is in accord with the time element in the development of late radiation reactions, since our average interval before the appearance of such reaction in the bladder was 2.5 years, and a fistula might represent an end-stage of this process. In the case of fistulas which developed in the presence of active disease, the average time of appearance was 1.6 years after the first treatment, and 0.75 years after the last treatment. A second but less likely tenet is that scar which follows regression of tumor after treatment, and which involves both bladder and vagina, may disintegrate to the point of fistula with the advent of serious infection.

It has been found also in our series, that fistula or radiation reaction are more likely to occur in those patients who have had treatment for carcinoma of the cervical stump, sometime after supravaginal hysterectomy. The reasons for this are evident and need no further discussion at this time.

There is apparent lack of agreement in the published reports concerning the incidence of vesicovaginal fistulas in carcinoma of the cervix. The figures of Warren, Williams, and Behney are in accord with ours. Smith, however, in presenting a large group of cases from the Memorial Hospital, stated that fistulas occurred with an average frequency of once in 98 patients (1.1 per cent). In his untreated group, there was an incidence of 7.2 per cent, though in his opinion this figure may be too low to represent the actual incidence since there was no attempt to follow closely those cases in which the disease was too advanced to be amenable to radiation therapy. With respect to the treated group, there may be several reasons for the wide difference in our figures. The ratio of the primary to the secondary or recurrent cases at the Memorial Hospital, estimated from Smith's data, was about 4.5 to 1, as compared to 1.8 to 1 at Pondville. Moreover, specific information concerning the extent of disease was not given. In our series, about 80 per cent were classified as C or D cases. It can be seen that these two facts, in themselves, indicating more advanced disease, may account for our higher percentage. The fistulas found at autopsy at the Memorial Hospital are not recorded, but it is probable that the figures would correspond closely to ours and those of others.

The difficulty of diagnosis in some instances in which the fistula is so small that it can be detected only by the introduction of dye into the bladder, or by postmortem examination must be borne in mind. Furthermore, repeated examinations until death cannot be made in many cases. As we have shown, fistula is an ominous sign and patients so afflicted frequently fail to return to the hospital and remain at home for terminal care. The absolute incidence of vesicovaginal fistula cannot be given. We believe that the figures presented by Smith are too low.

CONCLUSIONS

In conclusion, we believe that the bladder should be considered an integral part of the problem in carcinoma of the cervix, because of the great frequency with which it is involved by the disease itself, or as a result of treatment. We recommend cystoscopic inspection in the routine examination of all cases before instituting therapy and at intervals thereafter. By this means, when the bladder is found to be normal, a base line will be afforded for comparison with later observations as the case progresses. When, on the other hand, intravesical invasion is found to have taken place, the diagnosis as regards extent of disease at once will be rendered more accurate, and information of definite prognostic value will be obtained as well. It should be emphasized, however, that extension of disease into the bladder from the cervix should not be considered a deterrent to vigorous treatment of the malignant process. We have one unusual patient who had such extension even to the point of vesicovaginal fistula at the time of the first examination, and who now, after treatment, presents no evidence of active carcinoma. The fistula remains of course, but this is not too high a price to pay for successful cure.

BIBLIOGRAPHY

1. Aman-Jean, F. La vessie au cours de l'évolution du cancer de l'utérus. Bull. de l'Ass. franç. p. l'étude du cancer, 1933, 22: 556.
2. Colby, F. H. Urinary tract complications from uterine cancer. New England. J. Med., 1933, 209: 231.
3. Cutler, M. The treatment of carcinoma of the cervix with small quantities of radium. Surg., Gynec. & Obst., 1932, 55: 481.
4. Dax, L. Radium-nécrose tardive de la vessie après curie-therapie d'un cancer du col uterin. Rev. franç de gynéc. et d'obst., 1934, 21: 1005.
5. Dean, A. L., Jr. Ulceration of the urinary bladder as a late effect of radium applications to the uterus. J. Am. M. Ass., 1927, 89: 1121.
6. Idem. Injury of urinary bladder following irradiation of uterus. J. Urol., 1933, 29: 559.
7. Everett, H. S. Urologic complications following pelvic irradiation. Am. J. Obst. & Gynec., 1934, 28: 1.
8. Faerber, H. Woran Sterben die nicht operierten bzu. rezidiv gewordenen uteruskarzinomkranken. Ztschr. f. Geburtsh. u. Gynaek., 1931, 99: 213.
9. Findley, P. Complications resulting from pelvic irradiation. Am. J. Obst. & Gynec., 1935, 271: 358.
10. Fricke, R. E. Mortality study in carcinoma of uterine cervix treated by irradiation. Am. J. Roentgenol., 1935, 33: 670.
11. Haendly. Quoted by Schugt. Zentralbl. f. Gynaek., 1923, 47: 1262.
12. Hamann, A., and Gobel, A. Komplikationen bei der Radiumtherapie gynaekologischer Karzinome. Zentralbl. f. Gynaek., 1935, 59: 677.
13. Heimann, F. Bladder changes in inoperable carcinoma of the cervix before and after irradiation. Urol. & Cutan. Rev., 1927, 31: 58.
14. Kahn, I. Ulceration of the bladder simulating carcinoma, following the use of radium in the cervix. Urol. & Cutan. Rev., 1927, 31: 360.
15. Kleine, H. O. Zur Frage der Entstehung von Strahlen-Schadigungen infolge vorangegangener syphilitischer infektion (nach Radiumbestrahlung von Collum carcinomen syphilitischer Frauen). Arch. f. Gynaek., 1932, 149: 213.
16. Korkhov, V. Die Harnblase bei Strahlentherapie des Geboermutterkarzinoms. Zentralbl. f. Gynaek., 1934, 58: 681.
17. Liebhart, S., and Meisels, E. Ueber die sogenannten Spatschaedigungen nach Radiumbestrahlungen in der Gynaekologie. Strahlentherapie, 1931, 40: 508.
18. Marzetti, V. Le alterazioni della vesica nel cancero de colla dell 'utero. Clin. ostet., 1926, 28: 350.

19. MORTON, D. G. An autopsy study of women dying with cervical cancer after radiation. Calif. & West. Med., 1935, 42: 345.
20. NEWELL, Q. U., and CROSSEN, H. S. Late complications in irradiation treatment of cancer of the cervix. Surg., Gynec. & Obst., 1935, 60: 763.
21. OTTOW, B. Radiumschaedigungen von Harnblase und Darm. Ztschr. f. Geburtsh. u. Gynaek., 1930, 97: 121.
22. RULLE, P. Un cas rare de sequelles tardives après radiumtherapie. Gynec. et obst., 1929, 20: 720.
23. SANTY, P. Colpocléisis pour fistules vésicovaginalis consécutives à la radiumtherapie du cancer du col. Lyons chir., 1929, 26: 637.
24. SCHMITZ, H. Complications in the urinary tract due to carcinoma of the uterine cervix or radiation treatment. Am. J. Roentgenol., 1930, 24: 47.
25. SCHROEDER, C. Harnblase und Strahlentherapie des Uterus-carcinoms. Arch. f. Gynaek., 1932, 150: 147.
26. SCHUGT, P. Ueber einenfemerkenswerten Fell von Blasebutungen nach Roentgen Radium bestrahlung b. Zentralbl. f. Gynaek., 1923, 47: 1262.
27. SMITH, F. R. Incidence of vaginal fistulæ in patients with carcinoma of the cervix. Am. J. Cancer, 1934, 22: 52.
28. SMITH, G. G. Bladder reactions following application of radium to uterus. New England J. Med., 1932, 207: 822.
29. STACY, L. J. Complications following application of radium to pelvic lesions. Am. J. Roentgenol., 1928, 19: 323.
30. STRACHAN, A. I. Radiotherapy and fistula formation in cervical carcinoma. J. Obst. & Gynæc., Brit. Emp., 1931, 38: 542.
31. VERMOOTEN, V. Discussion of G. G. Smith's paper "Bladder reactions following application of radium to uterus." New England J. Med., 1932, 207: 822.
32. WAGNER. Der Geboermutterkrebs, eine pathologisch-anatomisch. Monographie. 2 Tafeln, 6: 169. Leipzig, 1868.
33. WARREN, S. Grading of carcinoma of the cervix as checked at autopsy. Arch. Path., 1931, 12: 783.
34. Idem. Personal communication.
35. WILLE, F. C. Radiumschaedigungen an Blase und Mastdarm bei Behandlung des Kollumkarzinoms. Monatschr. f. Geburtsh. u. Gynaek., 1930, 85: 383.
36. WILLIAMS, R. On morphology of uterine cancer. Brit. Gynec. J., 1895, 11: 529.
37. ZEISS, L. Beitrag zur Frage der Roentgen und Radiumschadigungen der Blase. Ztschr. f. Urol., 1927, 21: 626.

THE ROENTGEN TREATMENT OF TUMORS OF THE BRAIN OR SPINAL CORD IN THE OPERATING ROOM BY DIRECT RADIATION THROUGH THE OPEN WOUND[1]

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DURING the past decade, great progress has been made both in the surgical and the radiation treatment of infiltrating tumors of the central nervous system, but the combined results of surgery and radiotherapy still leave much to be desired.

Up to the present time, the greatest advances in the surgical treatment of tumors of the brain have been in the meningiomas and other relatively benign and encapsulated growths. The results of operations upon infiltrating growths have also improved, but there are many problems which remain to be solved.

The protoplasmic and fibrillary astrocytomas, especially those which occur in the cerebral hemispheres, are often solid infiltrating growths, and in many instances the tumor is so extensive that even by the excision of an entire lobe, all tumor tissue can not be removed.

When a glioma has undergone a cystic change and there is a discrete tumor nodule in the wall of the cyst, the evacuation of the cyst contents and the excision of the nodule has often given brilliant and lasting therapeutic results. This is especially the case in the cystic astrocytomas in the posterior cranial fossa that occur in childhood and early adult life. On the other hand, the astrocytomas that are found in the cerebral hemispheres are often solid growths and even if there are one or several large cysts, there is frequently no discrete tumor nodule. The solid part of the growth is often so large or so situated that it can not be completely removed. The statistics from a number of the neurosurgical clinics of this country, which were presented at a recent meeting of the Society of Neurological Surgeons, show that in many cases of supratentorial astrocytomas, life is prolonged for only 2 to 3 years. In some instances the survival period after operation is as long when little tumor tissue has been removed as after a gross total excision of the neoplasm.

When we turn from the astrocytomas and other rarer types of infiltrating tumor of the cerebral hemispheres, to the consideration of the rapidly growing and malignant glioblastoma multiforme, the picture is a still more gloomy one. The average length of life of a patient who has been operated upon for a multiform glioblastoma is often less than 1 year. Only in rare instances have the patients survived for a considerable number of years.

A similar story must be told concerning the surgical treatment of the medulloblastomas in the posterior fossa of children. The vascular base of this type of growth can practically never be removed, and a survival period of more than 2 to 3 years is unusual. These growths are radiosensitive, and the results of suboccipital decompression to relieve obstructive hydrocephalus and roentgenotherapy without removal of the growth appear to be as good if not better than radical extirpation.

The results of the removal of tumors of the spinal cord are much superior to those obtained by operations upon tumors of the brain, due to the fact that so many of the growths are benign, encapsulated, and extramedullary or extradural. In primary extradural malignant disease radical extirpation of the growth is often impossible, and only a small number of intramedullary tumors can be removed.

Therefore, in spite of the great advances that have been made, the best that can be accomplished by surgery in many tumors of the brain and some of the spinal cord is palliation and prolongation of life.

Most of the patients have received postoperative radiotherapy and the preceding statement applies to the results obtained by the combination of surgery and radiation therapy. It is not the purpose of the writers to discuss the subject of radiotherapy of tumors of the brain in detail, but to give a brief summary of the present status of the subject.

The use of roentgen radiation of tumors of the brain is based upon the known fact that the cells of many tumors are more radiosensitive than the normal brain or spinal cord. Opinions of roentgenologists differ regarding the sensitiveness to radiation of the various tumor types. That the medulloblastoma is very radiosensitive is well known, and the same is true of a certain number of solid pituitary adenomas. Although temporary clinical improvement after radiotherapy has been observed in many of the gliomas, there is little agreement on the question whether and to

[1] From the Surgical Division and Roentgen Ray Department of the Neurological Institute of New York.

what degree the cells of the tumors are affected by radiation. This subject was discussed in a symposium on radiotherapy of tumors of the brain at the meeting of the Association for Research in Nervous and Mental Disease in 1935. The various opinions there expressed may serve as a general summary of our present knowledge of the matter.

The conclusions of those who took part in the discussion were:

1. Radiation has an undoubted effect upon many tumors of the brain.

2. The degree of effect is not known, because there have been too few careful histological studies of tumor tissue before and after radiation.

3. There is little exact knowledge of the relation of the amount of radiation used to the results observed.

4. Profound changes in the tumor cells may be produced by roentgen therapy.

5. With the methods hitherto used, adequate doses of roentgen-rays can not be given because of the danger of injury to the soft and bony tissues of the head.

6. In a large proportion of the patients, the roentgen-ray dosage was inadequate.

The main object of this article is to suggest a method of procedure for the roentgen-ray treatment of irremovable or partially removable tumors of the brain and spinal cord, with which adequate dosage should be possible.

About 3 years ago it occurred to one of us that the roentgen-ray treatment of tumors of the brain or spinal cord could best be accomplished by the direct radiation of the growth at the time of operation when the brain and the tumor were exposed. This would become possible as soon as (1) high voltage x-ray machines had been devised so that the necessary time of exposure would be greatly shortened, and (2) as soon as a method of procedure had been worked out in which the radiation could be introduced directly into the tissue of the tumor at the time of the operation.

When the shock-proof high voltage x-ray machines were put on the market, the first condition aforementioned was satisfied. We then endeavored to obtain financial support for the installation in the operating room, of a new machine of this type. This support was only recently obtained. With the co-operation of the Picker X-ray Corporation, the plans for the installation of a high voltage machine in the main operating room of the Neurological Institute were completed, and the methods by which the personnel in the operating room would be completely protected against secondary radiations were worked out in the greatest detail. The machine has finally been installed and is ready for use.

In order to determine the maximum radiation to which the primate brain and spinal cord can be subjected without danger of injury to the nervous tissues, it is our purpose first to investigate carefully the effects of radiation on the exposed brains of monkeys. We have already subjected the brains of a few Macacus rhesus monkeys to prolonged radiation. All of the animals were under dial anesthesia. Under aseptic precautions a flap of the scalp was turned down, a large defect in the bone made with rongeurs and the dura widely opened. During the period of radiation, the exposed brain was covered with a piece of sterilized cellophane to prevent excessive drying and infection, and the remainder of the head and body protected by sterile leaded rubber sheets. After the radiation, the soft tissue flap was returned into place and the edges of the incision in the scalp united by Michel clips.

In one animal 2400 r units were given at one sitting directly into the exposed cerebellum and medulla. The monkey is apparently perfectly well more than 7 weeks after the operation and radiation. Another animal received 7200 r units in two equally divided doses one week apart into the left cerebral hemisphere. After these large doses, this monkey developed a complete right hemiplegia following the second radiation. Unfortunately, the animal died of a wound infection 5 days later. A third animal received 5400 r units in two doses into the left cerebral hemisphere and now, 14 weeks after the radiation, appears well except for a spasticity of the right upper extremity. These massive doses were given with an x-ray machine which could deliver only 20 r units in every minute. Therefore it was necessary to expose the animal's brain for from 2 to 3 hours at each sitting. This exposed the brain to an unnecessary amount of heat, drying, and risk of infection.

We propose to repeat these experiments with the new high voltage machine by which 60 r units per minute can be given. After a larger experience has been gained by animal experiments, it is planned to apply the method to human beings with irremovable tumors of the brain or spinal cord. Needless to say, great care and circumspection will be observed, and the effects of small roentgen-ray doses will be investigated before larger doses are used.

We have called this procedure "The Roentgen Treatment of Tumors of the Brain or Spinal Cord in the Operating Room by Direct Radiation Through the Open Wound." It will, of course,

require a long period of observation of the patients upon whom this procedure has been used before any statement can be made regarding the benefits and dangers of the direct radiation of the exposed tumor and brain. The sole object of this preliminary report is to call attention to a new method of procedure by which it is hoped that adequate radiation can be given directly into irremovable growths of the central nervous system and at the same time with a minimum of danger of injury to the soft and bony tissues of the head or trunk.

SUMMARY

The deficiencies of present day methods are:

1. The harmful effects to the skin and bone.

2. The fact that the tumor receives much less radiation than the skin.

The advantages of the proposed method are:

1. The maximum radiation will be given into the tumor.

2. The skin effects will be minimal.

NOTE.—Since this paper was sent to the Editor on May 22, 1936, a number of additional monkeys have been exposed to x-ray and several patients with tumors of the brain have received the therapy.

EDITORIALS

SURGERY, GYNECOLOGY AND OBSTETRICS

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1905–1935

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LOYAL DAVIS, M.D.....Associate Editor

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DECEMBER, 1936

TUBERCULOSIS OF THE BREAST

TUBERCULOSIS is one of the diseases to which the breast is not commonly subject but it cannot be considered rare. The incidence of tuberculosis of the breast in comparison with that of carcinoma of the breast, is respectively 1 case to 200 cases. There are two general types of tuberculosis of the breast. In the first, the disease is primary in the breast and in the second, it is secondary to tuberculous lesions elsewhere in the body.

Primary tuberculosis of the breast is rarely diagnosed clinically. The most common clinical diagnosis is carcinoma or purulent mastitis. The primary type of tuberculosis of the breast usually occurs in one of two forms: a diffuse form which may involve the greater part of the breast or a discrete form which is evidenced by a single tumor or by multiple tumors. In many instances it is impossible to distinguish tuberculosis from carcinoma of the breast, either by symptoms or by physical findings, for in the diffuse type of tuberculosis of the breast the lesion is hard, is irregular in outline, often is associated with edema and closely simulates the diffuse inflammatory type of malignancy. In the discrete type of tuberculosis of the breast there is often associated adenopathy and fixation of the lesion to the overlying skin; often there is no pain. Some features, however, if present, lead to the suspicion that the lesion is tuberculous. Usually mammary tuberculosis afflicts young women and the tumor increases in size more rapidly than a carcinoma. Although a tuberculous tumor of the breast usually is large when the patient presents herself for examination, metastasis is absent; if such a large growth were malignant, extensive metastasis would be demonstrable by physical or roentgenologic examination. Discharge from the nipple is more commonly a feature of tuberculous than of carcinomatous lesions and the discharge from a tuberculous lesion is usually composed of pus-like material whereas that from a carcinoma is serous or bloody. Retraction of the nipple is present if a tuberculous lesion is situated in the central portion of the breast, but this sign is not as common as it is in the presence of malignant lesions nor is it as marked. If tuberculous lesions are of long standing, an abscess may form and ulceration may take place. In such cases, the diagnosis usually can be established by examination of smears of the pus but the patients usually present themselves for examination before abscesses have formed or ulceration has appeared. The diagnosis in cases in which there is no draining sinus must be established by microscopic examination of the tissue after removal of the tumor. The

treatment is surgical. I believe the most conservative operation for primary tuberculosis of the breast to be simple amputation, followed by roentgen therapy applied over the regional lymph nodes. In some cases, in which the process is extensive and in which the axillary nodes are extensively diseased, complete axillary dissection will be required in addition to simple amputation. In cases in which the process is so extensive that the pectoral muscle and regional lymph nodes are involved, radical amputation is necessary.

Tuberculosis of the breast secondary to tuberculous lesions elsewhere in the body is usually diagnosed clinically because the primary lesion is recognized. The breast may be invaded either by way of the lymphatic channels or by direct extension, from an abscess in the thoracic wall to the tissue of the overlying breast. In many cases of this type there are draining sinuses and the diagnosis is easily established by examination of the pus. The surgical indication in cases of secondary involvement depends on the general condition of the patient, and in many instances all that is justified is general heliotherapy or roentgen therapy. In cases in which tuberculous abscesses of the thoracic wall invade the tissue of the breast, the best surgical treatment usually is simple amputation of the overlying breast and heliotherapy applied to the abscess or sinus of the thoracic wall.

STUART W. HARRINGTON

ANESTHESIA AND SURGERY

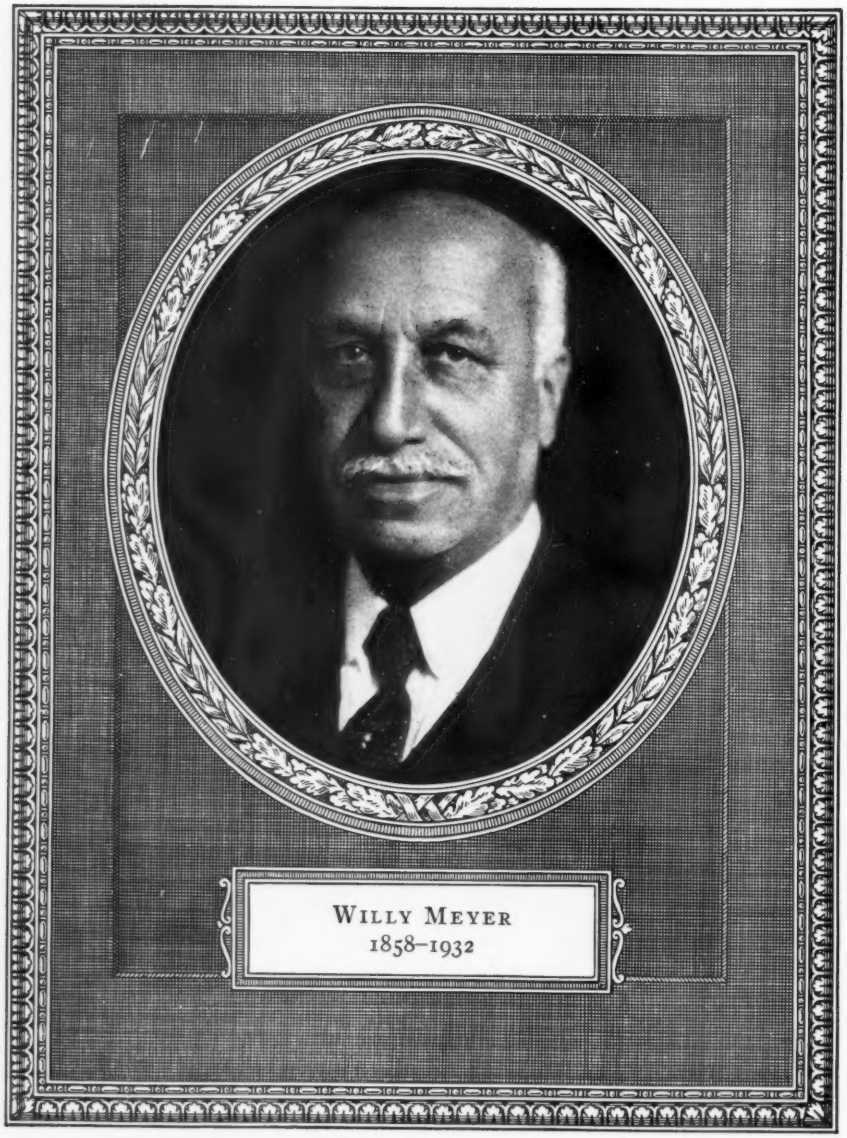
FROM the beginning of time means have been sought for, to allay pain and suffering. At first these attempts were crude and consisted mainly of pressure over blood vessels and veins, and the application of cold. The search was not limited to medical men. Through the ages progress was made, and in 1561 "the sweet oil of vitriol" is described in the writings of Valerius Cordis collected by Genser. The clinical use of ether had to await Long in 1842. The clinical art of anesthesia, the pharmacology and physiology of the anesthetic agents in use, was developed. This whole field was then placidly neglected by the medical profession except for the sporadic efforts of individuals. These individuals contributed the advances that were made to anesthesia up to the last two decades. Since that time the medical profession has again taken up anesthesia.

This placidity on the part of the medical profession was undoubtedly due to several factors: First, the anesthetic agents were one hundred per cent potent, covered every possible case, and with ether there was a wide margin of safety. In the second place, this potent anesthetic opened up the field of surgery so that surgeons were primarily interested in exploring these fields. The third factor was that these new fields served to occupy the attention not only of the surgeons but other fields of medicine; and anesthesia, because it got by, had to wait.

With this renewed interest on the part of medical men in anesthesia their work has resulted in advances in the science and the art. It has advanced so that the field of knowledge is so wide and its application in the clinical field so extensive that what has happened to anesthesia is the same story found in the other specialties of medicine and surgery.

To further the development close co-operation is an absolute necessity for progress. The anesthetist needs the co-operation of the surgeon, and the surgeon needs to understand this newer anesthesia so as to be able to give the patient the best possible service.

ERWIN R. SCHMIDT.



WILLY MEYER
1858–1932

MASTER SURGEONS OF AMERICA

WILLY MEYER

JUST before the close of a meeting of the New York Surgical Society, held at the Academy of Medicine on February 24, 1932, after he had finished discussion of a paper on "Cancer of the Breast," Dr. Willy Meyer was overcome by a sudden faintness due to a cardiac lesion from which he was known to suffer. Several of his colleagues came to his aid, but in spite of all efforts to revive him he succumbed.

It was a dramatic ending to the career of one of America's leading surgeons. His very presence at the meeting, and the circumstances attending it, were characteristic of him. He enjoyed attending meetings for the stimulus they gave him, and for the opportunity they presented of relating incidents from his vast experience. His discussions were always interesting and they were helpful to the younger surgeons, in that they sounded a note of optimism rather than pessimism. So on this, for him so fateful evening, when the subject for discussion was "Cancer of the Breast," a subject the treatment of which he had helped to develop, and to which he had devoted much thought, and of the curability of which he felt hopeful, he entered actively into the discussion. In his usual energetic way, he related the history of the development of the operation, cited cures of long standing, and sounded a note of hope for the victims of cancer, when he was stricken.

Dr. Meyer was a great surgeon, whose greatness did not lay in the performance of routine modern and popular operations, but in doing pioneer work in surgery. From early in his career until the very time of his death he was actively engaged in conquering one surgical condition after another. The qualities required for this he possessed to an unusual degree, he had an inquisitive mind, clear vision, indomitable energy, great ability, and excellent judgment.

Born in Germany on July 24, 1858, Dr. Meyer attended the Gymnasium at Minden and then studied medicine and graduated from the University of Bonn in 1880. After that he served as surgical assistant at this University until 1884, under the well known surgeons, Wilhelm Busch, Madelung, and Trendelenburg. In the fall of 1884 he came to America and engaged in general practice in New York City for 2 years. This served as a period of acclimation during which he became acquainted with conditions here. Having been trained in general sur-

gery, and feeling definite inclinations along that line, he soon devoted himself to that specialty. Beginning as an assistant in the surgical department of the German Dispensary, he rapidly rose to fame and was appointed to one important position after another. From 1886–1893 he was professor of surgery at the Woman's Medical College. In 1886 he was appointed attending surgeon at the New York Skin and Cancer, now the Stuyvesant Square Hospital, where he remained active until 1902. The longest periods of active service were devoted to the German, now the Lenox Hill Hospital, and to the New York Post Graduate Medical School and Hospital. In the former he served from 1886 until his retirement due to the age limit in 1923, while in the latter he served as attending surgeon and professor of surgery.

During more than 40 years of active practice one surgical problem after another engaged his attention and he never rested until he had mastered them. His early period of training fell into the important years when Lister's principles of antiseptic surgery were first applied. Then came the rapid advances of modern surgery based on this new knowledge, and Willy Meyer's work and his writings are intimately associated with this entire development.

Of his numerous contributions to the literature the first important one to attract general attention was the technique for the radical operation for cancer of the breast, published in 1894. Then came articles dealing with cystoscopy, urological surgery, modern gastric surgery, acute appendicitis, and many others.

There probably is no branch of surgery which did not engage the attention of Willy Meyer and about which he did not make some contribution to the literature. His mind was ever active and alert, and everything new which promised relief to suffering humanity was tried by him. The entire development of thoracic surgery in this country is intimately connected with his name. His was pioneer work in the true sense of the word, for in addition to the surgical problems involved, physical difficulties connected with pneumothorax had to be overcome. It took years of experimental work at the Rockefeller Institute, followed by its practical application in the thoracic pavilion of the German Hospital which helped to lay the foundation for thoracic surgery in America. Dr. Meyer was the founder of the New York Society for Thoracic Surgery as well as of the American Association for Thoracic Surgery.

During his entire professional life he was intensely interested in the subject of cancer. It found expression in the development of the radical operation for cancer of the breast, in numerous articles on the subject, and finally in his last great work, his book called *Cancer*, published in 1931. It speaks of the origin and development of cancer and deals with the therapy of operable and inoperable cancer in the light of a systematic conception of malignancy.

Willy Meyer's great activity has been of value not alone to the public, but to the younger men in the profession. He reached many through his writings

and through his lectures, and, because of his honesty and clearness in presenting a subject, and his note of optimism, he favorably influenced the career of many. Fortunate was the young surgeon who could serve under him, for he had the constant example of qualities which make for success, early rising, hard work, devotion to duty, careful observation, courage, ability, and consideration for the patient.

Dr. Meyer was married April 29, 1885, to Lilly Ottilie Maass, who died December 8, 1928. He is survived by two children, Marjorie Meyer Flemming, and his only son, Dr. Herbert Willy Meyer, who is "carrying on" in surgery.

Willy Meyer was respected by all and loved by many. His passing was a great loss to the profession, but his contributions to the development of surgery will live and they reveal that he truly left his

"Footprints on the Sands of Time."

CARL EGGERS.

LANDMARKS IN SURGERY

CHARLES BELL AND FACIAL PALSY

HARRY A. PASKIND, M.D., CHICAGO, ILLINOIS

CHARLES Bell, who possessed in such full measure the qualities of surgeon, investigator, philosopher, artist, and poet was born in Edinburgh in November, 1774. For 300 years there had been among his ancestors many men of learning and distinction. This strain of intellectuality found its fullest expression in Charles Bell and his brothers. The oldest of these, Robert, became the author of the Scotch law dictionary; the next, John, was to become the celebrated surgeon; the third, George Joseph, was to be elected professor of law in the University of Edinburgh; and Charles was destined for accomplishments of such splendor and magnitude as to lead to perpetual fame and renown.

In later years, referring to his early education he wrote, "I received no education but from my mother; neither reading, writing, ciphering nor anything else. My education was the example set me by my brothers; there was in all the members of my family a reliance on self—a true independence—and by imitation I obtained it. People prate about education and put out of sight example, which is all in all."

John Bell, his brother, had gained a reputation as an anatomist and surgeon; he decided to take Charles under his tutelage and teach him the elements of anatomy and of surgery, and at the same time allow him to take courses at the University of Edinburgh. Here the youthful Charles fell under the influence of some of the unusual men on the faculty of Edinburgh University of that day. Of these probably the most striking was Dugald Stewart, a man of magnetism and sound intellect who occupied the chair of philosophy. Young Bell also studied with Black, who succeeded the great Cullen as professor of chemistry, and who was called by Foulcroy the Nestor of chemical revolution. At the University, Bell also fell under the influence of Alexander Monro, the celebrated anatomist, and James Gregory, the internist, who as a teacher was conspicuous for a sound practicality, and who often brought forward the maxim, "The best physician is he who can distinguish what he can do from what he cannot do." During this period Bell was coached by David Allan, the artist, who helped Bell develop his ability to draw, a talent which was first observed and nurtured by his mother.

In 1789, while still an undergraduate, he published his *System of Dissections* with plates engraved from his own sketches, and wrote the description of the nervous system in John Bell's *Anatomy of the Human Body*.

On August 1, 1789, Charles Bell, having completed his course at the University, was admitted to the Edinburgh College of Surgeons, and immediately afterward he was appointed to the surgical staff of the Royal Infirmary, the only hospital in Edinburgh. Here he soon became known for his remarkable skill as an operator; dexterity, simplicity, originality, and dispatch characterized his work. At this period he began to model pathological specimens in wax, and soon had an extensive collection of which some remarkable specimens may even at the present time be seen in the museum of the College of Surgeons in Edinburgh.

SIR CHARLES BELL
1774–1842

After an altercation with Gregory, Charles Bell and his brother were not reappointed to the infirmary; Charles decided that Edinburgh afforded him insufficient opportunity, and he left Edinburgh to pursue his career in London.

On a Sunday late in November of 1804 Charles Bell arrived in London. It was a discouraged, defeated, homesick Bell that walked the streets of London on that Sunday. Regarding his first day's experiences in London he wrote, "If this be the season that John Bull selects for cutting his throat, Sunday must be the day, for then London is in all its ugliness, all its naked deformity, the houses are like ruins and the streets deserted."

During the early period of his life in London the only encouragement that he received was an

invitation to join the Anatomical Society. The London anatomists, having heard of him through his "Dissections" and his chapters in John Bell's *Anatomy*, invited him to join their society. This served to acquaint him with the most prominent English anatomists of that day—Cline, Cooper, Abernethy, Home, Wilson, Baillie, and Blizard; and although their reception of Bell was at first lukewarm and condescending they soon became his friends. These new friendships encouraged him but little, for at this time he wrote to his brother: "I can make a few good friends, but I cannot engage the multitude." Gratifying as was his membership in the Anatomical Society it still left him without a place to work.

Unable to find an opening in an institution already established, Bell decided that he had to found one of his own. So on January 20, 1806, he took a house on Leicester Street, Leicester Square, and fitted it up as a lecture room and living quarters, and decided to establish himself as a lecturer.

Bell's lectures met with unqualified success, and his fame as a lecturer spread rapidly throughout London; more pupils were attracted and more patients sought him out. By 1808 he had thirty-six paying pupils while the professor at the Royal College of Surgeons had only four.

In 1812 Wilson offered him a partnership in the Great Windmill-Street Medical School. The school was founded by the Hunters, and was the scene of their great success. Bell accepted this offer with alacrity. His anatomical and pathological preparations and his drawings were added to the collection already there, much to his joy. His first lecture in this school was attended by 100 pupils.

Honors now came thick and fast. Bell was admitted to the Royal College of Surgeons in 1813. The next year he was elected surgeon to the Middlesex Hospital, and he early began to make great use of the opportunities that this hospital afforded. His lectures and operations here were attended by students and eminent practitioners; his practice now grew very rapidly.

Bell was appointed professor of anatomy in the Royal College of Surgeons in 1824. By this time his fame became so widespread that his lectures were crowded to suffocation. From 1827 to 1830 he took a prominent part in the founding and development of the University College (now London University), but here he was allowed insufficient freedom, and he resigned from the College in 1830. In 1831 the order of Guelphic knighthood was conferred upon him and he became Sir Charles Bell. In 1835 the Council of Edinburgh elected Sir Charles to the chair of surgery at Edinburgh University; he accepted the offer and that year returned to the scene of his early labors.

Bell entered London in 1804, unknown, ignored, almost insolvent, and a Scotchman (a word almost opprobrious in the London of the day), and he left London in 1835, famous, sought after, highly solvent, and an English knight. His rise was due in part to his brilliance as a lecturer, anatomist, and surgeon, but infinitely more to the brilliant discoveries forever to be associated with his name.

In 1811 he published *A New Idea of the Anatomy of the Brain*. In this work he relates an experiment performed on an ass in which irritation of the posterior root caused pain and irritation of the anterior root convulsion of the muscles of the back. "I now see," he writes "the meaning of the double connection of the nerves with the spinal marrow."

In 1813 Bell concluded that strabismus ought to be relieved surgically by cutting the nerve to the intact muscle responsible for the deviation of the eyeball. He had his assistant, Shaw, look all over London for a cross-eyed monkey. Bell could not be induced to make this first experiment on a human being. Shaw brought back a monkey but it was not cross-eyed. In default of a squinting monkey, Bell decided to try section of the facial nerve on this animal. DuBois d'Amiens describes this event as follows, "The poor animal began to grimace with redoubled energy, but entirely on one side of his visage, the other remaining quite motionless. No one, assuredly, could have thought of practicing this experiment upon a human being, but nature took it upon herself. All who were admitted to see the monkey operated on by Charles Bell, were struck with the strange analogy its physiognomy presented with that of an old actor then high in repute in London, who could at pleasure express every variety of passion on one side of his face, while the opposite half exhibited no emotion whatever. Charles Bell's experiment supplied him with a clue to the enigma. It was found that this comedian, struck by facial hemiplegy, in consequence of an accidental injury to the motor nerve, simply availed himself of a natural infirmity." This was the accouchement of the expression, "Bell's palsy," a term applied today to paralysis produced by peripheral lesion of the facial nerve.

In 1806 he published *The Anatomy of Expression*, a book widely read by physicians and used as a text by artists. One year later appeared his *Operative Surgery*, and in 1810 *Disease of the Urethra. Engravings from Specimen of Morbid Parts* was published in 1813, and in 1814 he wrote a work on gunshot wounds. Then appeared in rapid succession his *Surgical Observations*, *Essay on the Forces which Circulate the Blood*, and *Observations on Injuries of the Spine*.

Sir Charles Bell returned to Edinburgh in 1835. Edinburgh did not, however, give him the satisfaction that he had hoped for, although his classes there were successful. Practice in Edinburgh did not yield what it did in London and the honorarium at the University did not make up for this deficiency. His fellow professors were somewhat cold to him; he interpreted this as Scotch undemonstrativeness and not as "jealousy." "I have a German professor to breakfast," he wrote at this time, "who brings me a volume from Paris—they make me greater than Harvey. I wish to heaven the folks at home would make something of me."

On April 27, 1842, Sir Charles and Lady Bell stopped at Hallow Park, the country seat of his friends, Mr. and Mrs. Holland, near Worcester. Here he enjoyed the scenery and made several sketches of the yew trees in the vicinity. That day he said to his wife, "This is a novel spot; here I would rest till they come to take me away." After dinner the same evening he sketched various medical celebrities of his acquaintance, admired and discussed Leonardo da Vinci's "Last Supper." In a happy mood he said to his wife, "Did you ever see me happier or better than I had been this forenoon?" These remarks were evidently intended to keep his wife from worrying, because that day he had had several paroxysms of anginal pain and that very evening his face became pale several times. Before bedtime he read aloud the "Twenty-Third Psalm," then retired and fell into a deep, quiet sleep. In the morning he awoke with severe pain, which he said was due to changing his position. His wife arose to give him some laudanum. Calling her to him, he laid his head on her shoulder and died.

No more fitting tribute has been paid to Sir Charles Bell than that in the *Edinburgh Review* for April, 1872. "Never passed away a gentler, truer, or finer spirit. His genius was great and has left a legacy to mankind which will keep his name fresh in many generations. But the story of his life has a more potent moral. It is the story of one who kept his affections young, and his love of the pure unsullied, while fighting bravely the battle of life; whose heart was as tender as his intellect was vigorous and original, who, while he gained a foremost place amongst his fellows, turned with undiminished zest to his home and his friends and found there the object, the reward, and the solace of his life."

Sir Charles was buried near a yew tree that he had sketched a few days before in Hallow Churchyard. At first a plain stone with his name, dates of birth and death, and the line, "The pure in heart shall see God," marked the spot. Afterward a tablet was placed in the churchyard with an inscription by his lifelong friend and schoolmate, Francis (Lord) Jeffrey. It reads, "Sacred to the memory of Sir Charles Bell, who, after unfolding with unrivalled sagacity, patience, and success, the wonderful structure of our mortal bodies, esteemed lightly of his greatest discoveries, except only as they tended to impress himself and others with a deeper sense of the infinite wisdom and ineffable goodness of the Almighty Creator."

THE SURGEON'S LIBRARY

REVIEWS OF NEW BOOKS

THE two volume work entitled *Operative Gynecology*[1] written by H. v. Peham and J. Amreich has been translated into English by L. Kraeer Ferguson, of the University of Pennsylvania. It includes a charming foreword from the pen of the late Dr. George Gellhorn who writes "we have been greatly in need of a treatise on operative gynecology which would be a worthy successor to Kelly's classic of 35 years ago. . . . An operative gynecology should impart the three essential requisites of a good surgeon . . . a sound anatomic knowledge . . . technical skill and refinement of execution and . . . wise surgical judgment."

The first volume of 245 pages is divided into two parts, "a description of the methods and materials which are essential to . . . a successful performance of all gynecologic operations . . . and the surgical anatomy of the female pelvis." In the second volume various gynecological operations are described and illustrated in detail throughout their several steps. The results of some of the authors' investigative studies as well as statistical compilations from their own experiences are here recorded for the first time. They preferred to report these data in their text rather than crowd them into periodicals even though such a policy has sometimes cost them priority in the literature.

In the first portion of volume 1 the following subjects are considered: asepsis and antisepsis, anesthesia, postoperative complications and their prevention, hemorrhage and hemostasis, opening the abdomen, and finally pre-operative and postoperative treatment in gynecological surgery. In the second portion, on the anatomy of the female pelvis, the authors consider pelvic connective tissue, the ureter, arteries of the genital system, arteries of the rectum, veins of the genitalia, the lymphatics of the pelvic organs, and nerves.

In volume 2 one finds a discussion of the indications for operation and the choice of procedure in various types of pelvic pathology. Next the authors describe and handsomely illustrate the detailed technique of the various operations which they employ and finally each chapter is concluded by a statistical résumé of their own personal experiences and end-results after utilization of the operations as described. The following lesions are considered: carcinoma of the cervix, carcinoma of the body of the uterus, myoma, extra-uterine pregnancy, pelvic inflammatory disease, tuberculosis, ovarian tumors, prolapsus, retroversion, complete perineal tear, aplasia of the vagina, bladder and ureteral fistulas, rectovaginal and rectovesicovaginal fistulas, sphincter weakness with incontinence, bartholin cyst, kraurosis vulvæ, carcinoma of the vulva, and appendicitis.

As one reads these volumes and studies the illustrations he is impressed that the authors are original in their presentation. They describe only those procedures which they employ and they attempt to justify their choice of operations by citing the results which have been obtained in their own patients. They are thorough and explicit in every description; being convinced of the pedagogical soundness of repetition, this characteristic of their style of presentation was not at all disturbing. The illustrations are the forte of this text—they appeal to the eye, they are accurate and detailed, they are original and they are offered in such profusion that the anatomy of the female pelvis and the details of operations are unfolded in an enviable and enlightening manner.

Peham and Amreich's *Operative Gynecology* is an enduring contribution to our gynecological texts and books of reference. It contains a wealth of information for every gynecologist, young or experienced; look and see for yourself. It should grace the library of every surgeon who operates for pelvic pathology because of its lucid presentation of pelvic anatomy. Finally, no surgeon can afford to be deprived of immediate access to the illustrations of the abdominal and vaginal operations for cancer of the cervix, or the operation for cancer of the vulva.

GEORGE H. GARDNER.

VOLUME VII of *Pathologie und Klinik in Einzeldarstellungen*[2] is an important study of cretinism by the professors of surgery and pathology of the University of Bern. The work of these men in the center of the Swiss goiter area has fitted them by years of first hand clinical and pathological experience with cretins to render an authoritative account. Wegelin discusses the history and endemiology. DeQuervain describes the clinical findings in general and, in detail, the changes found in the various systems of the body. Wegelin, from an extensive pathological material, presents the anatomy

[1] OPERATIVE GYNECOLOGY. By H. v. Peham and Dr. J. Amreich. With introduction to the edition in English by George Gellhorn, M.D. Authorized translation made by L. Kraeer Ferguson, M.D., Vols. 1 and 2. Philadelphia, Montreal, and London: J. B. Lippincott Company, 1934.

[2] PATHOLOGIE UND KLINIK IN EINZELDARSTELLUNGEN. Edited by L. Aschoff, H. Elias, H. Eppinger, C. Sternberg, K. F. Wenckebach. Band vii. Der endemische Kretinismus. By Prof. Dr. F. de Quervain and Prof. Dr. C. Wegelin. Berlin and Vienna: Julius Springer, 1936.

of all of the tissues. DeQuervain reviews the pathological physiology of protein, mineral, and carbohydrate chemistry, respiratory metabolism, blood and blood cell changes, the blood proteins, iodine excretion and blood iodine, liver function, and thyroid function. The authors combine in presenting a study of the pathogenesis of cretinism. This interesting chapter analyzes the importance of various factors in the production of cretinism—the distinction between athyreosis and cretinism is stressed. Every student of thyroid disease should have this valuable presentation. PAUL STARR.

BOOKS RECEIVED

Books received are acknowledged in this department, and such acknowledgment must be regarded as a sufficient return for the courtesy of the sender. Selections will be made for review in the interests of our readers and as space permits.

THE OXFORD MEDICINE. By various authors. Edited by Henry A. Christian, A.M., M.D., LL.D., Sc.D.(Hon.). Vol. 7. PSYCHIATRY FOR PRACTITIONERS. New York: Oxford University Press, 1936.

PROCTOLOGY; A TREATISE ON THE MALFORMATIONS, INJURIES AND DISEASES OF THE RECTUM, ANUS AND PELVIC COLON. By Frank C. Yeomans, A.B., M.D., F.A.C.S., M.R.S.M.(Lond.Hon.). 2d ed. New York and London: D. Appleton-Century Co., 1936.

TEXTBOOK OF SURGICAL NURSING. By Manelva Wylie Keller, B.S., R.N. 3d rev. ed. New York: The Macmillan Co., 1936.

THE EMANCIPIST; AN HISTORICAL DRAMA. In Three Acts. By Maj.-Gen. John Macquarie Antill, C.B., C.M.G., and Rose Antill-de Warren. Sydney: Angus & Robertson Ltd., 1936.

DISEASES OF THE AIR AND FOOD PASSAGES OF FOREIGN-BODY ORIGIN. By Chevalier Jackson, M.D., Sc.D., F.A.C.S., LL.D., and Chevalier L. Jackson, A.B., M.D., M.Sc.(Med.), F.A.C.S. Philadelphia and London: W. B. Saunders Co., 1936.

THE EGGS OF MAMMALS. By Gregory Pincus. New York: The Macmillan Co., 1936.

A TEXTBOOK OF OBSTETRICS. By Edward A. Schumann, A.B., M.D., F.A.C.S. Philadelphia and London: W. B. Saunders Co., 1936.

TRANSACTIONS OF THE PACIFIC COAST SOCIETY OF OBSTETRICS AND GYNECOLOGY. Vol. v, Year 1935. Edited by Albert Mathieu, M.D. Portland, Oregon: The Western Journal of Surgery, 1936.

THE CLINICAL USE OF DIGITALIS. By Drew Luten, A.B., M.D. Springfield, Illinois, and Baltimore, Maryland: Charles C. Thomas, 1936.

DISEASES OF THE TESTICLE. By Hamilton Bailey, F R.C.S.(Eng.). London: H. K. Lewis & Co. Ltd., 1936.

ROENTGEN INTERPRETATION; A MANUAL FOR STUDENTS AND PRACTITIONERS. By George W. Holmes, M.D., and Howard E. Ruggles, M.D. 5th rev. ed. Philadelphia: Lea & Febiger, 1936.

UROLOGY; FOR NURSES. By Oswald Swinney Lowsley, M.D., F.A.C.S., and T. J. Kirwin, M.D., F.A.C.S. Philadelphia, London, Montreal: J. B. Lippincott Co., 1936.

ANATOMY OF THE HUMAN BODY. By Henry Gray, F.R.S. 23d ed., thoroughly revised and re-edited by Warren H. Lewis, B.S., M.D. Philadelphia: Lea & Febiger, 1936.

LIVE LONG AND BE HAPPY; HOW TO PROLONG YOUR LIFE AND ENJOY IT. By Lewellys F. Barker, M.D. New York and London: D. Appleton-Century Co., 1936.

THE 1936 YEAR BOOK OF RADIOLOGY. DIAGNOSIS. Edited by Charles A. Waters, M.D. Associate Editor: Whitmer B. Firor, M.D. THERAPEUTICS. Edited by Ira I. Kaplan, B.Sc., M.D. Chicago: The Year Book Publishers, Inc., 1936.

OXFORD MEDICAL PUBLICATIONS. PSYCHIATRY FOR PRACTITIONERS. By various authors. Edited by Henry A. Christian, A.M., M.D., LL.D., Sc.D.(Hon.). (Reprinted from Oxford Loose-Leaf Medicine.) New York: Oxford University Press, 1936.

MOTHER AND BABY CARE IN PICTURES. By Louise Zabriskie, R.N. Philadelphia, Montreal, London: J. B. Lippincott Co., 1936.

OSNOVI AKUSHERSTVA. By V. Shtekkel.

OXFORD MEDICAL PUBLICATIONS. PAGET'S DISEASE OF THE NIPPLE; AND ITS RELATION TO SURFACE CANCERS AND PRECANCEROUS STATES IN GENERAL. By Keith Inglis, M.D., Ch.M.(Sydney). London: Oxford University Press, 1936.

THE INTELLECTUAL FUNCTIONS OF THE FRONTAL LOBES; A STUDY BASED UPON OBSERVATION OF A MAN AFTER PARTIAL BILATERAL FRONTAL LOBECTOMY. By Richard M. Brickner, B.S., M.D. New York: The Macmillan Co., 1936.

EUGENICAL STERILIZATION; A REORIENTATION OF THE PROBLEM. By The Committee of the American Neurological Association for the Investigation of Eugenical Sterilization. New York: The Macmillan Co., 1936.

UROLOGY. By Edward L. Keyes, Ph.D., F.A.C.S., F.R.C.S.(Hon. Eng.), and Russell S. Ferguson, A.B., M.D. 6th ed. New York and London: D. Appleton-Century Co. Inc., 1936.

TEXTBOOK OF GENERAL SURGERY. By Warren H. Cole, M.D., F.A.C.S., and Robert Elman, M.D. New York and London: D. Appleton-Century Co. Inc., 1936.

MODERN UROLOGY; IN ORIGINAL CONTRIBUTIONS BY AMERICAN AUTHORS: Edited by Hugh Cabot, M.D., LL.D., C.M.G., F.A.C.S. Vol. i, GENERAL CONSIDERATIONS—DISEASES OF PENIS AND URETHRA—DISEASES OF SCROTUM AND TESTICLE—DISEASES OF PROSTATE AND SEMINAL VESICLES. Vol. ii, DISEASES OF THE BLADDER—DISEASES OF THE URETER—DISEASES OF THE KIDNEY—RADIATION THERAPY OF TUMORS OF THE GENITO-URINARY TRACT. 3d rev. ed. Philadelphia: Lea & Febiger, 1936.

A TEXTBOOK OF SURGERY. By John Homans, M.D. 4th ed. Springfield, Illinois, and Baltimore, Maryland: Charles C. Thomas, 1936.

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